



*Presented to the*  
LIBRARY *of the*  
UNIVERSITY OF TORONTO  
*by*  
Miss Jean Robinson







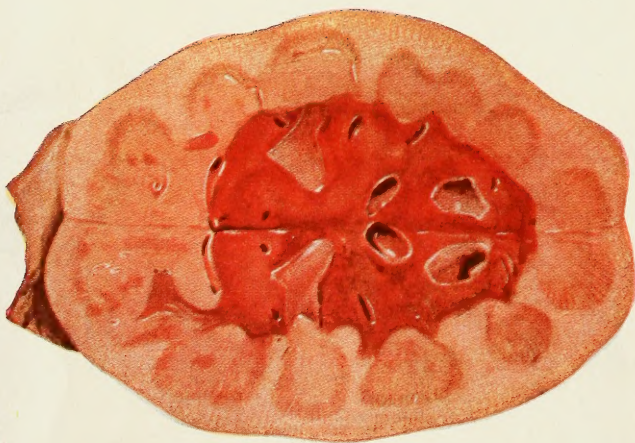








# PLATE I.



Colored drawing of the right kidney as it appeared, when cut open, soon after the necropsy. It shows the position of the red myeloid (and hemorrhagic) tissue at the hilus, filling up the space between the kidney substance and renal pelvis, normally occupied by connective tissue and fat. The kidney substance looked paler when the kidney was first cut into. The appearances in both kidneys were identical.

(*Quarterly Journal of Medicine*)



Microscopic colored drawing (about the same magnification) from another piece of the tissue occupying the renal hilus. It shows three remaining fat vesicles, with erythrocytes (hemorrhage) and myeloblasts (or "non-granular myelocytes"). The section was stained by Leishman's method.—Weber, page 259.



*The*  
***Practical Medicine Series***

COMPRISING EIGHT VOLUMES ON THE  
YEAR'S PROGRESS IN MEDICINE AND SURGERY

---

*Under the General Editorial Charge of*  
**CHARLES L. MIX, A. M., M. D.**

*Professor of Physical Diagnosis in the Northwestern  
University Medical School*

---

***Volume I***

***General Medicine***

EDITED BY

**FRANK BILLINGS, M. S., M. D.**

*Head of the Medical Department and Dean of the Faculty of  
Rush Medical College, Chicago*

WITH THE COLLABORATION OF

**BURRELL O. RAULSTON, A. B., M. D.**

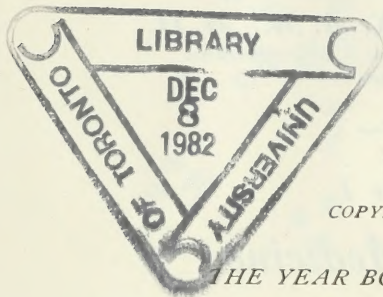
*Assistant Attending Physician and Resident Pathologist,  
Presbyterian Hospital, Chicago*

---

**SERIES 1920**

---

CHICAGO  
THE YEAR BOOK PUBLISHERS  
304 South Dearborn Street



R  
101  
Y39  
1920

COPYRIGHT 1920

BY

THE YEAR BOOK PUBLISHERS

# TABLE OF CONTENTS

---

	PAGE
PROGRESS OF MEDICINE.....	7- 26
Intravenous Injection of Foreign Protein.....	24- 26
INFECTIOUS DISEASES .....	27-257
Contagion .....	27- 30
Tuberculosis .....	30- 62
Influenza and Influenzal Pneumonia .....	63-120
Colds .....	120-123
Pneumonia .....	124-146
Meningitis and Meningococcus Infections .....	146-163
Poliomyelitis .....	163-164
Rheumatism and Arthritis .....	165-176
Malaria .....	176-190
Typhoid and Paratyphoid Fevers .....	191-199
Dysentery .....	200-217
Yellow Fever .....	218-226
Sand-Fly Fever .....	226-227
Trench Fever .....	227-228
Measles .....	228-234
Mumps .....	234-237
Pertussis .....	237-238
Smallpox .....	238-240
Cholera .....	240-243
Anthrax .....	243-248
Tetanus .....	248-252
Rabies .....	253-257
DISEASES OF THE MEDIASTINUM .....	258-262
DISEASES OF THE BRONCHI AND UPPER AIR PASSAGES .....	263-284
Asthma .....	265-278
Bronchiectasis .....	278-281
Bronchial Spirochetosis .....	281-284



# CONTENTS

	PAGE
DISEASES OF THE LUNGS AND PLEURAE .....	285-309
DISEASES OF THE HEART AND BLOOD-VESSELS ..	309-370
Aneurysm .....	356-359
Aortic Disease .....	359-365
Angina Pectoris .....	365-370
DISEASES OF THE BLOOD AND BLOOD-MAKING	
ORGANS .....	371-395
Blood Transfusion .....	371-381
Filariasis .....	381-382
Bacteremia .....	382-383
Anemia .....	383-388
Diseases of the Spleen .....	388-395
DISEASES OF THE DUCTLESS GLANDS .....	396-444
The Thyroid .....	396-427
The Thymus .....	427-428
The Suprarenals .....	428-434
The Hypophysis .....	434-438
The Pineal Gland .....	439-440
The Lymphatic Glands .....	440-444
DISEASES OF METABOLISM .....	445-457
DISEASES OF THE KIDNEY .....	458-491
DISEASES OF THE GASTRO-INTESTINAL TRACT ..	492-589
Gastric and Duodenal Ulcer .....	528-556
Sarcoma of the Stomach .....	556-562
Syphilis of the Stomach .....	562-563
Botulism .....	563-566
Intestinal Parasites .....	566-580
Intestinal Obstruction .....	580-582
The Cecum .....	582-584
Colitis .....	584-589
DISEASES OF THE LIVER AND GALL-BLADDER ..	590-600
DISEASES OF THE PANCREAS .....	601-603
MISCELLANEOUS DISEASES .....	603 611

# GENERAL MEDICINE

## PROGRESS OF MEDICINE

**Treatment of Chronic Malignant Diseases.** A recognition of local and general resistance as guides in the treatment of certain chronic malign affections, is the title of an article by J. L. Yates,<sup>1</sup> of Milwaukee.

He states that the epithet "malignant" is applied in a pathologic sense to denote metastasizing neoplasms, and these are commonly believed to be inevitably lethal unless destroyed, root and branch, by some form of treatment. In determining whether or not surgical treatment has cured a malignant tumor, it must be remembered that there may be a long latent period, twenty-six years, between operation and final metastatic activity, hence, there is no possible arbitrary time limit to establish a cure.

In addition to tumors of this malignant type, there are the chronic granulomatous affections which are held, or at some time have been held, to be quite as commonly lethal. For example, a group, recognized under the name of Hodgkin's disease is believed to be irrecoverable, and is considered by some to be a granuloma, by others to be a neoplasm, and by still others a granuloma with a tendency to provoke malignant metamorphosis of tissues involved, endothelial, lymphoblastic or fibrous.

There is good reason, the author says, from a therapeutic aspect to collect into one group those morbid processes which provoke similar defensive actions, although the etiology and proportion of consequent fatalities show a wide dissimilarity. Studies of chronic surgical affections of this type conducted with the intimate co-operation of Dr. C. H. Bunting have led Yates to a tentative inclusion in such a group of the following:

1. Tumors: (a) Carcinoma, (b) endothelioma, (c) lymphoblastoma (Mallory), (d) lymphosarcoma, (e) mesothelioma.

(1) Wisc. Med. Jour., September, 1919.

2. Granulomas: (a) Tuberculosis, (b) Hodgkin's disease, (c) lymphocytic leukemias, (d) actinomycosis, (e) blastomycosis.

The object in treating disease is not to cause a disappearance in its manifestations, but to eradicate the cause. No one may present evidence of successful treatment and expect it to go unquestioned if the process at the time treatment was begun had not assumed the characteristics that established its lethal nature were it left untreated, and if a careful necropsy made years later failing to show a trace of the original process is not included.

Adequate treatment must be based on physiologic reactions and must offer to each individual every opportunity to complete recovery, and must not be biased by any successes, real or apparent, attained by short-cut methods. No single form of treatment by surgery, radiation, serum, hygiene or internal medication has yet been found to be sufficient in this class of disease. A coördination of all these therapeutic agents now seems to offer the best chances, with, of course, the usual exceptions.

The general plan for treating these granulomatous conditions includes the following:

In the first place there must be elimination of irritants. The primary focus or portal of entry should be destroyed permanently by the most suitable means, knife, cautery, or radiation or combinations of these methods. The regional area of lymphatic glands and gland-bearing tissue should be extirpated accurately. Any other accessible involvement should be similarly treated, so long as the patient's general condition warrants it, because such a focus becomes in effect a primary focus.

The conservation of local defenses depends on protections of local resistance, which, after elimination of a specific irritant is attained, depends on the character of repair that follows extirpation. This will be satisfactory in proportion to the integrity of blood and nerve supply, and to the reduction of limitations of function by avoidable fibrous tissue formation.

Great advantage can be obtained from radiation after operations.



Properly given, the *x*-ray can destroy toxin-forming cells that operation fails to remove. It can retard the regeneration of lymphatic structure until destruction of the offending cells or organisms has been accomplished and thus reduce the danger of local recurrence. It can also do great damage: not only locally by burns, by provoking serious hemorrhage and by interfering with healing, but also by its effect on the body. Whatever may be found to be the explanation, radiation of the circulating blood can produce profound changes in the blood, particularly in causing a reduction in the lymphocytes.

The persistence of a high lymphocyte count has proved to be the most reliable single proof of a high state of general resistance in these diseases. A rapid and persistent fall in the number of lymphocytes has regularly heralded approaching disaster. It is possible that these observations may explain the occasional stimulation of malignant activity by the *x*-ray. For this reason the dosage and periodicity of treatments should be controlled in part by the blood reactions.

The third point in this general plan of treatment is the maintenance of unimpaired general resistance. The real problems lie in this field, which has been woefully neglected because attention has been centered upon the physical to the neglect of the physiologic aspect, and because of a wondrous superstition that the omnipotent surgeon completed the treatment at operation.

Facts tell us that in these conditions the hygienic measures are no less important than in the after-care of patients discharged with arrested diseases, from a tuberculosis sanitarium.

Drugs are of use, not as specific remedies, but as tonics, stomachics, laxatives, etc.

In this attempt to maintain the general condition in a good state, a special effort should be made to avoid everything known to depress lymphoblastic activity as indicated by the lymphocytes in the blood-stream, an exception being the presence of hyperlymphocytosis.

Finally, Yates emphasizes again that the blood picture, and particularly the lymphocytic elements therein, is the best single index for estimating general resistance and therefore in controlling treatment.

Observations on the progress of malign affections as influenced by methods of treatment here outlined have, in spite of many failures, shown in the few favorable results abundant justification for a growing optimism in the ability of combined therapeutic efforts to prevent, to cure and to alleviate these stubborn diseases.

**Clinical Diagnosis as Compared with Necropsy Findings.** A study of the findings in 600 necropsies constitutes the basis of an article by Howard T. Karsner, Leonard Rothschild and E. S. Crump,<sup>2</sup> of Cleveland.

The cases were equally divided between two large hospitals in Cleveland. The results are classified by organs and symptoms, rather than by special lesions. There were certain marked errors of diagnosis that defy any such classification. These have been classified as gross errors, and the authors have not included any instances in which the clinical diagnosis, even though markedly in error, was of the same organ found in these at necropsy. They have included certain very obvious errors of omission. This group numbers fifty of the 600 cases, or 8 per cent. A few examples, serving to illustrate the type of error included in this group are given in Table I:

TABLE I—ILLUSTRATIVE EXAMPLES OF THE TYPE OF "ERROR OF OMISSION" IN CLINICAL DIAGNOSIS

Clinical Diagnosis	Pathologic Diagnosis
Lobar pneumonia .....	Cerebral tumor; no pneumonia
Acute endocarditis .....	Acute peritonitis from ruptured pus-tube; no endocarditis
Lobar pneumonia .....	Epithelioma of larynx; tuberculosis right upper lobe; no pneumonia
Typhoid fever .....	Lobar pneumonia
Carcinoma of stomach.....	Lobar pneumonia; no stomach lesion
Cardiovascular disease .....	Carcinoma of stomach
Cerebrospinal syphilis .....	Acute pyelonephritis
Acute alcoholism .....	Fracture of skull
Tuberculous meningitis .....	Bronchopneumonia
Aneurysm of descending aorta..	Atrophic cirrhosis; rupture esoph- ageal vein
Cirrhosis of liver.....	Lobar pneumonia; cloudy swelling of liver
Carcinoma of stomach.....	Pulmonary tuberculosis; amyloid liver and spleen; no lesion of stomach

(2) Jour. Amer. Med. Ass'n, Aug. 30, 1919.

Those errors in which the affected organ was properly diagnosed have been classified as minor errors, thus including here the errors of commission. In addition, this group has been made to include the failure to observe the lesions of the special organs. Many of these errors are not so serious as to justify inclusion in the "gross errors"; but in order to make the figures more accurate, it is necessary to include with each organ, cases which also have been classified above as "gross errors." The total number of correct diagnoses have been compared with the total number of cases diagnosed, and thus an estimation of percentage of error of commission has been obtained. Minor errors are tabulated in Table II; the figures in this table apply only to the organs and systems included in the table:

TABLE II—MINOR ERRORS

Organ or Part of Body	Cases Diagnosed	Correct Diagnoses		Cases Over- looked	Chance of Correct Diagnosis
		No.	Per Cent.		
Head and brain.....	72	43	60	7	54
Heart and pericardium....	119	62	52	36	47
Lungs and pleura .....	174	95	54	77	38
Position of lobar pneumonia	68	25	37	12	31
Liver and biliary tract....	30	17	57	17	36
Gastro-intestinal tract .....	66	36	54	8	49
Non-suppurative nephropathy	60	46	77	72	34
Blood-vessels .....	36	24	67	21	42
Totals for these organs.	625	348	56	192	40

The authors state that if clinical diagnosis in a large community, well and favorably known for its medical investigation and teaching, is subject to an 8 per cent. factor of gross error and a 60 per cent. factor of minor error, it is reasonable to suppose that similar chances of error exist in less favored communities. This can not be interpreted as a failure on the part of the clinician to give his cases proper attention and therapy, for many of the minor errors disclosed had no influence whatever on the treatment of the case or its outcome. To differentiate all the cases in which the errors in diagnosis would influence the outcome presupposes knowledge of the in-

tricacies of natural adaptation to disease which science at present does not possess.

The improvement of clinical medicine depends, however, on increasing accuracy of diagnosis, from which a more rational therapy may be adduced. The exact benefit of improvement in the diagnosis and the treatment of diseases of man to his productive labor can be estimated only from morbidity statistics, which have never been accurately tabulated for any large group of people. The improvement must be along lines of more exact clinical study, and can be properly controlled almost solely by recourse to the postmortem examination of carefully studied patients. The service of such examinations is not only to the medical profession, but directly to the public.

In conclusion the authors say that investigations of the cause of this general shortcoming of American medicine in studying the accuracy of clinical diagnosis lead to a variety of explanations and an equal variety of suggestions for improvement. The latter may be summarized as follows:

There should be education of the public as to the importance of postmortem examinations to public health.

Improvement of legislation: (*a*) obviation of the necessity for written permission to perform a necropsy, and (*b*) recognition of the difference between anatomic dissection and the necropsy.

Improvement of hospital regulations.

Increased development of the interest of physicians in the necropsy.

Encouragement of the "selfish interest in postmortems on the part of intelligent relatives of the dead."

Assignment, in large hospitals, of certain persons whose special duty it shall be to secure permission for postmortem examinations.

Information given the family as to the conditions discovered by the necropsy.

A request for necropsy in every fatal case in hospital or private practice.

Establishment in the hospitals of regular clinical pathologic conferences.

**The Influence of Desiccation on Human Normal**

**Isohemagglutinins.** The practical importance of human normal isohemagglutinins in determining the suitability of prospective donors for the transfusion of blood has been emphasized many times. The quest for an accurate, rapid and convenient method of determining the compatibility of donor and recipient has led to the development of a large number of methods to supercede the older, time-consuming methods described in the various text-books.

As a means of saving time and affording a greater convenience, Sanford has recommended the use of dried serum. He allowed the serums to dry in air on cover-slips, after which they were wrapped in paper and kept in the ice-box. For grouping an unknown blood, the dried drops of serums of Groups II and III, were dissolved in one drop of the cell suspension, and the grouping made according to the classification of Moss. He observed that the serums still possessed marked agglutinating properties after more than two months. Karsner noted that in France there seemed to be a deterioration and loss of specificity of the agglutinins a short time after they were dried. This observation led Howard T. Karsner and Herbert L. Koeckert<sup>3</sup> to carry out a series of experiments in order to determine whether or not the use of these dried smears is reliable. They experimented with dried serum of known agglutinin titer. The serum was allowed to dry on cover glasses, kept under various conditions, and tested at seven-day intervals for twelve weeks. The conclusions reached as a result of this work were as follows:

Normal human iso-agglutinins exhibit deterioration within from two to three weeks and loss of group specificity within from three to five weeks after drying, regardless of the method of desiccation employed or the previous addition of a preservative or the elimination of salts by dialysis.

Complete loss of specificity with coincident acquisition of non-specific agglutinating power occurs within from seven to ten weeks after desiccation.

The agglutination of corpuscles of all groups by a serum that has lost its specificity for particular groups

(3) Jour. Amer. Med. Ass'n, Oct. 18, 1919.



emphasizes the agglutinative power of serum to be far more important in the mechanism of agglutination than the agglutinability of the corpuscles, and refutes the assumption of specific iso-agglutinophilic substances.

There is a considerable reduction in the agglutinin titer by the redissolving of dried serum in enough distilled water or physiologic sodium chloride solution to restore the original volume.

The use of undried serum, put up in small capillary tubes, is a most convenient, rapid and economical, as well as accurate, method for grouping blood.

**Relation between Feeding Yeast and Antibody Production.** An attempt to determine the effect of feeding yeast on antibody production in animals has been made by Elizabeth Pauline Wolf and Julius Herman Lewis.<sup>4</sup>

The work was undertaken with the view of a possible explanation of the therapeutic value claimed for yeast in infectious diseases. Various workers have emphasized the efficacy of yeast in the treatment of furunculosis and other staphylococcus infections. They have given no explanation for its action, but suggest that the laxative value combined with some fixed effect on the intestinal tract may be the cause of improvement that follows its use.

Since all the diseases for which yeast is said to be a specific are induced by staphylococcus, streptococcus and other pyogenic organisms, and since the recovery from these diseases is due to an increased antibody production, it is logical to suspect that if it has any beneficial action, its influence is on the yield in antibodies. In order to determine whether this is true or not, the authors studied the effect of feeding yeast on the production of antibodies to sheep blood-cells in rabbits. They had in mind also the possibility of discovery and isolation of a substance which specifically increases the production of antibodies, an accomplishment not yet attained, but the importance of which has been realized in clinical medicine. The experiment was made three times with a new series of animals each time.

The conclusions reached in this work were, in brief, that the feeding of yeast had no stimulating effect on the

(4) Jour. Infect. Dis., October, 1919.



production of antibodies to sheep blood in rabbits. The production of antibodies was even less than in controls. No evidence was found that yeast has any effect on the gastro-intestinal tract of rabbits.

### **Presence of Filter-Passing Virus in Certain Diseases.**

During the autumn of 1917 and the spring and summer of 1918, observations were carried out by Sir John Rose Bradford, Capt. E. F. Bashford and Capt. J. A. Wilson<sup>5</sup> on the pathology of acute infective polyneuritis. These resulted in the detection, isolation and culture, by the Noguchi method, of an organism that reproduced the malady inoculated into animals and, further, this organism was recovered by culture from such experimental animals.

The results accomplished in this investigation led to the application of the same methods to other diseases. The present article is a preliminary report of the presence of a filter-passing virus in other diseases, especially trench fever, influenza and nephritis.

The virus isolated in trench fever consisted of minute coccus-like bodies, grouped in pairs, with the opposing surfaces flattened and varying in size from  $0.3\ \mu$  to  $0.5\ \mu$ . It was Gram-positive and stained readily if the film preparations were washed in ether before the stain was applied. It passed through Berkefeld N. and V. filters, and also through Massen porcelain filters and could be cultivated from such filtrates. It resisted heating to a temperature of  $56^{\circ}\text{C}$ . for 30 minutes, and it was an anaërobe.

This organism was recovered by culture from the blood in eleven out of fifteen cases of trench fever examined during the pyretic stage, and in three out of eight cases when apyretic. It was not found in over forty control cases in which blood cultures with the same technique were carried out.

A similar organism was recovered in four separate supplies of infected louse excreta. It was not found in thirty-one specimens of excreta from batches of clean lice.

---

(5) *Lancet*, Feb. 1, 1919. An abstract of a later article by these authors on "The Filter-Passing Virus of Influenza" appears on page 80, this volume.

The cultures obtained either from the blood of man or from louse excreta, when inoculated by scarification into man, produced a mild illness, and the organism could be recovered from the blood by cultures during such illness, and also from clean lice fed on the patients during the illness.

The virus isolated in cases of influenza consisted of a very minute, rounded, coccus-like body varying from 0.15 to 0.5  $\mu$ . It was Gram-positive and passed through Berkefeld N. and V. filters and Massen porcelain filters. It was an anaërobe and resisted heating to 56° C. for 30 minutes. It was isolated by culture from the blood in six out of nine cases examined, from the sputum in six out of six examined, from the pleural fluid in four out of four examined, and from the cerebrospinal fluid in the only case so examined. It was isolated from the lymphatic glands at postmortem in the only two cases examined. This organism could not only be grown from the blood and from exudates, but it could also be seen in stained film prepared from exudates; for example: sputum, pleural fluid, and cerebrospinal fluid. The cultures (second generation) when inoculated into animals subdurally or intravenously produced illness in guinea-pigs and monkeys, and on postmortem examination the lesions found resembled those produced by the original disease. The organism was recovered by culture from the tissues of such experimental animals.

Up to the time that this paper was written, only one variety of nephritis had been investigated; *i. e.*, that characterized by the presence of pyrexia and hematuria at the onset. The virus isolated in such cases of nephritis consisted of a round coccus-like body, varying from 0.3  $\mu$  to 0.6  $\mu$  in size, and in culture often occurred in the form of short chains of four individuals.

The same organism was seen in urinary sediments distinctly or in pairs. It was Gram-positive, and passed through Berkefeld N. and V. filters and also through the Nassen porcelain filters. It was an anaërobe and resisted heating to 56° C. for 30 minutes. It was isolated from the blood in six out of nine cases examined, and from the urine in seven cases. The cultures (second generation) when inoculated into animals produced

nephritis in monkeys and guinea-pigs. In monkeys this could be determined not only by postmortem examinations but also clinically, since the urine contained blood, albumin and casts. In both guinea-pigs and monkeys extensive lesions, glomerular and tubular, were found on microscopic examinations. In severe cases pulmonary lesions were also present. The organism was recovered by culture from the tissues of the animals experimentally inoculated.

These three diseases are those that were most studied, but organisms of the same group, although differing from one another, were recovered by culture in a number of other diseases of obscure etiology. Among the most important diseases, in which true filter-passing organisms were isolated by culture in the blood and seen in suitably stained films, mumps, measles, rose measles and typhus are mentioned.

An organism allied apparently to that of polyneuritis, was isolated from brain tissue in certain cases of encephalitis lethargica, both from material obtained from England, and also from cases observed in the army in France.

**The Regulation of the Acid-Base Equilibrium of the Human System.** This discussion of the mechanism for the regulation of the acid-base equilibrium of the system and its bearing on clinical medicine by W. F. Litchfield,<sup>6</sup> of Sydney, Australia, is presented with such clearness, that a large portion of it must certainly be of interest and value to those who can not read extensively on this particular subject. No apology is offered therefore for taking large parts of this article as they are presented by the author.

It has been estimated, says Litchfield, that the hydrogen-ion concentration of pure water is 1.0 gram in 10 million liters, and that the hydrogen-ion concentration of the blood is 0.4 gram in 10 million liters, hence, if water be regarded as the standard of neutrality, then blood is a slightly alkaline fluid.

The human organism is very sensitive to acids, and life and function depend, within quite narrow limits, on the reaction of the blood and tissues, to such an extent indeed that an increase of the hydrogen-ion concentra-

---

(6) Med. Jour. Australia, Feb. 15, 1919.

tion of the blood to 1 gram in 10 million liters promptly causes death. Acids such as carbonic, hydrochloric, phosphoric, sulphuric, oxybutyric, oxalic and lactic are being continually formed in metabolism. It is of moment, therefore, to consider how the normal reaction of the blood is maintained.

The general principles of this research are now well understood, owing to the work of Haldane, Henderson, Barcroft, Moore, Lewis, Palmer, Van Slyke and others. Under ordinary circumstances, the introduction of base in the food, the elimination of carbon dioxide by the lungs, the excretion of acids by the kidneys and, probably, to a less extent by the skin, and the utilization of urea ammonia in saving base serve to keep the reaction of the blood constant.

The first line of defense is formed by the bicarbonates, chiefly sodium bicarbonate, of the blood. The bicarbonate has the power to hold carbon dioxide in the proportion of one to twelve without any sensible change in reaction. This is in response to the chemical laws governing the combination of strong bases to weak acids.

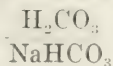
Recently Buckmaster has adduced strong evidence in favor of hemoglobin being an important carrier of carbon dioxide in the blood, and Moore holds that plasma and tissue proteins can hold acids to a certain extent without a sensible change in reaction. In these ways, some or all of them, without any strain or circulatory disturbance, a stream of acid, the equivalent of several hundred cubic centimeters of pure hydrochloric acid, passes out of the system every twenty-four hours. Furthermore, the respiratory center is extremely sensitive to variations in the acid content of the blood, and any increase of carbonic acid gas, such as occurs during exercise, promptly excites the respiration to increased action, and thus leads to its elimination. Carbonic acid used to be regarded as the respiratory hormone, but Henderson declares the hydrogen-ion to be the true exciter of the respiratory center, and indeed, it must be so since it is the hydrogen-ion that establishes acidity in any case. One may recall here the similarity between the catalytic action of acids and that of enzymes. The bicarbonates of the blood also act as buffer salts to acids.

When any acid—as lactic acid—is formed in metabolism and finds its way into the blood, it combines with the sodium salt to form sodium lactate, and release carbonic acid, which can not only be easily driven off by the lungs, but is a much weaker acid than lactic, in that its electrolytic dissociation is far less. The proteins of the plasma and tissues are also said by Benjamin Moore and others to act as buffer substances to acids and alkalies, by virtue of their amphoteric character, being able to take up and hold a certain amount of acid or alkalies when these are in excess in the blood.

The next important part of the mechanism is the excretion of acids by the kidneys. Acids formed in metabolism immediately claim bases and form salts. Some acids, such as oxybutyric and phosphoric, are excreted in the free state, the base being returned to the blood. The most important action of the kidney in this respect, however, is its capacity to alter the ratio of the excretion of alkaline and acid phosphates. When there is the necessity of saving base in the system the acid phosphate of sodium  $\text{NaH}_2\text{PO}_4$  is excreted in preference to the alkaline, sodium phosphate  $\text{Na}_2\text{HPO}_4$ . It has been shown that in normal subjects the kidneys eliminate from 200 to 800 c.cm. tenth-normal acid in twenty-four hours. The base excreted as salts in the urine is replaced by base in the food.

Next is the part played by ammonia in neutralizing acids. The formula of urea is  $(\text{NH}_2)_2\text{CO}$ , and the system has some power of utilizing the  $\text{NH}_2$  before it is converted into urea to neutralize acids, thus saving bicarbonate of soda and other alkalies.

Henderson sums the matter up this way: The hydrogen-ion concentration of the blood depends on the ratio—



If acid reduces the denominator, the respiratory center is stimulated and the lungs reduce the numerator; further, ammonia releases base and the kidneys remove a greater proportion of acid phosphate, thus returning base to the blood.

From what has been said, it is clear that the organism



has many resources for maintaining the normal reaction of the tissues, and that Nature in this respect, as in others, works with a wide margin of safety.

Nevertheless, acidosis, owing either to excessive production or deficient excretion of acids, does occur. Henderson says it is as common as fever and should be tested for clinically in pathologic states. Acidosis may be defined as a depletion of the alkali reserves of the body, and especially of the bicarbonates of the blood.

Hyperpnea is the only positive clinical symptom of acidosis, but this is a late and severe manifestation. Tests for acetone and diacetic acid may show these substances in the urine but these bodies, while they are important, only indicate one form of acid production, namely, that from the incomplete oxidation of fats, moreover they may recur in easily demonstrable quantities without diminishing the bicarbonate reserves of the blood, and further, there may be severe acidosis in their absence. An increased ratio of ammonia to urea nitrogen in the urine may indicate an acidosis, and is a useful test. The determination of concentration of bicarbonate in the blood is another way to uncover an acidosis. This may be done in three ways:

1. By estimating the amount of  $\text{CO}_2$  in the alveolar air.
2. By determining the carbon dioxide capacity of the blood by Van Slyke's method.
3. By giving by the mouth 5 grams of bicarbonate of soda and watching the effect on the urine.

Of these methods, the best for practical purposes seems to be Van Slyke's, and it is desirable that clinical laboratories should be in a position to supply Van Slyke's readings. There is a full account of his apparatus and method in Joslin's book on the treatment of diabetes published recently.

Haldane and Priestly showed the intimate connection between the carbon dioxide tension in the alveolar air, and therefore in the blood and respiratory activity. It became evident that this effect was due to the stimulating or sensitizing effect of carbonic acid on the respiratory center. Then it was observed that other acids, such as lactic acid, after severe exercise, and oxybutyric acid



in diabetic coma, had a stimulating effect on the respiratory center, and now it seems to be accepted that it is the hydrogen-ion that is the chemical factor which in conjunction with certain peripheral nerves controls the respiration.

The relation of the chemical and nervous factors in respiration may be stated as follows: Deflation or negative ventilation of the lungs excites inspiration, inflation or positive ventilation excites expiration, and the hydrogen-ion concentration determines the amount of response. The hydrogen-ion concentration in blood is 0.4 gm. in 10,000,000 liters, that is, one part in 25,000,000,000, and yet the very slightest increase has a profound effect on the respiratory center.

But, it must be asked: does the action of hydrogen-ion stop with the respiratory center? It is established that any increase of acidity in the blood has a stimulating effect on general metabolism, and one can not see any good reason why other centers in the medulla, such as the sweat center and vasomotor center, should not share in the stimulating effect of the hydrogen-ion. It may be that acid has some controlling influence on metabolism in general, and it can be seen that the stimulation of metabolism by acid would, like the stimulation of the respiratory center, be a protective measure in acidosis, by ensuring a complete combustion of the products of metabolism and the proper elimination of acid bodies. However, that is for the future.

The acidosis in diabetes is due to acetone, diacetic acid and oxybutyric acid, also known as ketone bodies.

The following are some of the facts known about these substances. If a normal man lives for three days on a carbohydrate-free diet his urine will react for acetone and diacetic acid. Total fasting for one or two days will also cause their appearance in the urine. Prolonged fasting does not lead to their notable increase, and in cases of diabetes fasting leads to their disappearance. Acetone and its allies occur in patients suffering from persistent vomiting. They are frequent in the first days of acute illness in children, due probably to temporary starvation. In a diabetic patient the increased consumption and combustion of carbohydrate causes a diminution

or disappearance of ketone bodies. These facts make it appear that the formation of the bodies is controlled in some way by the combustion of carbohydrate in the body.

A diabetic patient may secrete large quantities, Joslin says several hundred cubic centimeters, in twenty-four hours. The best treatment for acidosis in diabetes is starvation, preceded, if coma is threatened, by a vegetable diet containing 5 to 10 per cent carbohydrates for two or three days. Theoretically, large doses of bicarbonate of soda should be of benefit, but they are rarely successful in curing diabetic coma, and Joslin is doubtful of their value.

In cyclic vomiting and delayed chloroform poisoning, acidosis due to ketone bodies occurs, and may cause some of the symptoms of these conditions.

The question of the value of giving alkalis in acidosis is important. At first sight it would seem that, as the alkaline reserve of the body is reduced in such cases, the administration of bicarbonate of soda could only do good. The matter is not so simple, however. In health the system has its own way of regulating the reaction of the tissues, and no doubt there is a rhythm in the mechanism of the excretion of acids, as witness the alkaline (morning) and acid (evening) tides first spoken of by Sir William Roberts. In disease a new equilibrium, with an altered rhythm, is probably established. Acid supplies the stimulus for its own elimination and alkalis may diminish the stimulus and upset the balance. In chronic nephritis, for instance, the night hours see a large excretion of urine brought about by the acid tide, and large doses of alkali might easily alter this and lead to the retention of salts of a harmful nature. Clinically, it is known that alkalis are not well tolerated in chronic Bright's disease. In acute Bright's disease, on the other hand, alkalis do good. Eitchfield has treated acute nephritis in children with large doses (about 12 grams daily) of potassium citrate, and the results have been excellent. It is plain, however, that discretion is needed in administration of alkalis.

It should be remembered also that acidosis is secondary to some nutritional disturbance or error of metabolism.

All the states in which acidosis occurs seem to have one thing in common, namely, exhaustion or fatigue.

**The Production of Tetany with Sodium Bicarbonate.** The production of tetany by the intravenous infusion of sodium bicarbonate in an adult is recorded by George A. Harrop, jr.,<sup>7</sup> of the Medical Clinic of the Johns Hopkins Hospital.

The patient was a colored woman, 22 years old. On the day of her admission to the hospital, before she had taken any food, she swallowed two 7½ grain tablets of bichloride of mercury, dissolved in a glass of water. From the time of her admission to the hospital, a few hours after taking the bichloride, the patient passed blood in the urine and stool. She had already vomited blood in appreciable quantities. The usual energetic measures were taken to secure a large fluid intake and to eliminate the mercury.

On the day following admission to the hospital, the woman became totally anuric and continued so until death. On the day following admission she was given 500 c. c. of a 5 per cent. sodium bicarbonate solution intravenously. Twenty-four hours later, she was given another intravenous infusion of 700 c. c. of a 5 per cent. solution of sodium bicarbonate. Following this second injection, about five minutes after it had been completed, the patient developed a well-defined attack of tetany which lasted about fifteen minutes. Some of the symptoms of tetany, however, lasted for as long as twenty hours after this initial attack. No definite convulsions were observed during any of this time. The patient died ten days after admission to the hospital.

Harrop states that he was unable to find any clinical reports of tetany occurring in adults following administration of sodium bicarbonate. Among the many incidents following its use in the treatment of diabetic coma, the occurrence of convulsions, especially of clonic type, is frequently mentioned. These convulsions have usually led to a rapidly fatal termination, often in a few hours. Tetany, however, has not been mentioned or identified as such. Howland and Marriott have recorded tetany in young children following the thera-

(7) Bull. Johns Hopkins Hosp., March, 1919.

peutic administration of sodium bicarbonate for acidosis, and they cite three cases. During the period of tetany their patients showed a low calcium content of blood serum, a condition which they have shown to be present during the active period of infantile tetany, particularly during or shortly after the occurrence of convulsions. In the present case, however, the calcium and phosphate content of the blood was determined, and in each instance was found to be practically normal. Harrop considers it clear that the conditions observed in the patient in this instance were associated with if not directly precipitated by the suddenly increased alkalinity of the blood due to the sodium bicarbonate infusion.

The author therefore directs attention to a danger, not too remote, attendant upon the intravenous use of sodium bicarbonate in conditions in which the renal excretory function is markedly impaired and particularly when extreme oliguria or anuria is present.

## INTRAVENOUS INJECTION OF FOREIGN PROTEIN

**Protein Therapy.** Cassini<sup>8</sup> defines this subject as follows: This is a method of treatment in which one utilizes certain proteins in the management of disease, chiefly infections, and which is wider than the conception involved in proteose or peptone therapy in that it can include any substance which contains protein and is used in the treatment of disease. Thus, transfusion of blood is listed under the head of protein therapy. The subject dates back to Koch's original tuberculin and includes the work of Wright on opsonins in vaccine therapy. Beginning with bacteriotherapy the next stage comprises the use of bacillary extracts which are albumoses, and this initiated the study of various proteins. A mixture of albumoses and bacilli (typhoid) has been used with success in treatment of typhoid fever. Milk was used but later given up on account of the danger of fat embolism. Later, Nolf devised his peptone injection for the treatment of typhoid, which gave an impetus to other forms of protein therapy.

(8) Gaz. des Hôp., Nov. 8, 1919.

At present, the following have been used: whole blood, plasma, serum, milk, substances classed as albumoses, substances classed as peptones, polypeptides.

Blood, with or without preliminary treatment, is of course of value besides the protein content, as a reconstituent. The intravenous injection is the method of choice for protein therapy. The diseases that have responded with good results are typhoid, typhus, influenza, tuberculosis, erysipelas and scarlatina (streptococcus). Of the non-specific groups, hemorrhage is the principal one to be treated in this manner.

The arthritides, and especially those due to the gonococcus, have been treated in this manner. The vegetable proteins are not used, although boiled milk intramuscular injections have been used with success by this author.

**Intravenous Injection of Peptone in Infectious Diseases.** In the treatment of infectious disease both experimental and clinical Nolf<sup>9</sup> has administered peptones by mouth, intravenously, subcutaneously and intramuscularly. He advocates the subcutaneous injection of peptones in the pupuras and also in paroxysmal hemoglobinuria *a frigore*. He believes that it can be employed successfully to combat meteorism as in typhoid. When peptone is injected into the veins of a dog one can often see, as a result, contraction of the small intestine. The author employs 3 ctg. of dry peptone per kilogram of body weight by the intravenous route. The total not to exceed 1.5 gm. of peptone dissolved in 200 c. c. of isotonic salt solution. After one or two hours there is a violent and prolonged chill, with a temperature of from 40.6° C. to 42° C. After one hour the temperature begins to fall and within twenty-four hours it becomes normal. There is a marked improvement in the general condition, and the meteorism disappears. The reaction is distinct, and the results very marked.

Nolf states that he has employed this method in a number of severe typhoid cases with success. In a close analysis, one observes an immediate result and a subsequent reaction. The immediate reaction depends upon the amount of peptone injected. If one injects from 5

(9) Presse méd., Feb. 24, 1919.



to 6 ctg. there is only a slight rise of temperature after the injection, with return to normal after two or three hours. If the amount of protein is large there is a distinct rise in the temperature, a severe chill lasting from twenty to thirty minutes, and marked perspiration or even shock. In some cases it is necessary to repeat the injection of peptone after two or three days, but in repeated doses one must be on the alert for anaphylaxis. Whether one injects vaccines or peptones the reaction is dependent upon hydrolysis of the protein molecule.

[The intravenous injection of any foreign protein, in sufficient amount to cause reaction, is followed by a severe chill, immediate leukopenia, then by fever, sometimes hyperpyrexia, polynuclear hyperleukocytosis, and great general discomfort and suffering. The reaction varies in degree with the dosage and to some degree with the foreign protein used. The same dosage of typhoid bacillus protein will cause less reaction than the protein of the colon bacillus. The result of the treatment in typhoid fever, pneumonia and other acute infections and in chronic diseases is not constant. The *modus operandi* of the treatment is not understood. The method is not free of danger. If used, the doses should be small and the risk should not be taken without due deliberation. —B.]



## INFECTIOUS DISEASES

### CONTAGION

**Droplet Infection and its Prevention by the Face Mask.** The part played in the transfer of infectious diseases, infection by mouth, droplets driven out in forced expiratory efforts, has not usually received sufficient attention. The tendency of those who have insisted on the almost exclusive rôle of contact infection in the spread of contagious diseases has been to include droplet infection among the forms of contact infection, but to assign it a minor part.

This state of affairs has led to careful scientific investigation and among others, George H. Weaver,<sup>1</sup> working in the McCormick Memorial Institute for Infectious Diseases, Chicago, makes a valuable contribution to the subject.

He states that recent experiences in this institution have emphasized the fact that carriers and droplet infections are two factors which must receive a large share of attention in the management of contagious diseases. Intimate contact of individuals is essential in order that droplet infection may occur, and this applies equally to single persons and to large numbers in camps, crowded cars or public gatherings within doors.

Important facts bearing on this phase of the spreading of disease are that tubercle bacilli have been found in the saliva and on the tongue in a considerable proportion of cases of pulmonary tuberculosis. Diphtheria bacilli have been found on articles contaminated by saliva from persons with diphtheria. Teague is quoted as having found diphtheria bacilli in the saliva of 77 per cent. of cases in which tonsillar cultures were positive. This same finding has been confirmed by Weaver in his work. In any cases in which pathogenic organisms are present in the pharynx, nasopharynx, and in sputum

(1) Jour. Infect. Dis., March, 1919.

from the deeper respiratory passages, it is likely that the mouth will be more or less contaminated by them and that they will be in the saliva.

The occurrence of infection after exposure to mouth spray depends on several factors, especially the immunity of the individual and the number of bacteria taken in. Immune individuals may become carriers without exhibiting any evidence of infection. The distance to which mouth droplets are carried in the air depends principally on the force with which they are driven. While some workers claim that the danger zone about a coughing patient has at least a ten foot radius, the author's experience would indicate that relatively few bacteria pass more than a few feet from the patient in ordinary coughing in the absence of currents of air.

At the Durand Hospital, as a part of the John McCormick Memorial Institute for Infectious Diseases, where this investigation was carried out, rigid aseptic methods have been followed, and the nurses have been specially instructed in measures calculated to protect them from infection. From March 12, 1913, to Nov. 1, 1914, nine out of sixty-nine nurses, or 13 per cent., acquired clinical diphtheria. From this time on, all nurses giving a positive Shick test were immunized with diphtheria antitoxin. This practically eliminated active diphtheria, but from Nov. 1, 1914, to June 1, 1916, weekly throat cultures disclosed ten diphtheria bacillus carriers among forty-three nurses, or 22.25 per cent. Up to June 1, 1916, nine cases of scarlet fever occurred among 112 nurses on duty, or 8 per cent. In an attempt to explain these high instances a special effort was made to eliminate infection through mouth spray. From June 1, 1916, gauze masks were used by the nurses and up to Oct. 1, 1918, six diphtheria carriers were detected among seventy-three nurses, or 5.2 per cent. No case of scarlet fever has occurred since masks have been worn. The nurses are instructed to change the mask as soon as it has been known to be grossly contaminated and never to put the hands to the mask to adjust it, etc., until they have been thoroughly washed.

In order to determine the value of masks, experiments were carried out to determine how much of a given dye,

and how many bacteria in a salt solution suspension would pass through gauze masks of varying thicknesses, and size of mesh. The results of these experiments are conclusive, and have influenced the staff at Durand in adopting the mask shown in the accompanying illustration (Fig. 1).

With the addition of this protective measure at this institution, there has been noted a considerable reduction in cases of rhinitis, tonsillitis, and pharyngitis among the



Fig. 1. Directions for making the Durand Hospital Mask. Devised by Miss Charlotte Johnson, Supt.

1. Cut (44 by 40 mesh) gauze 8 inches wide and 23 inches long.
2. Turn down sides and one end  $\frac{1}{4}$  inch. Fold twice, unturned end first, making  $7\frac{1}{2}$  inch square.
3. Cut off opposite diagonal corners 1 inch and turn in raw edge  $\frac{1}{2}$  inch. Stitch firmly all around.
4. Take up a 1 inch dart  $1\frac{1}{2}$  inches long at middle of each side of mask. Sew 14 inch tape on opposite uncut corners.

This mask has the advantage of covering the nose and mouth and in making the traction on the chin and not drawing on the nose and lips.

nurses. Endeavors to limit droplet infections should not prevent equally energetic efforts to close other channels of spread of infectious materials. The use of face masks

should not give an unwarranted feeling of security to those employing them and lead to neglect of the measures which prevent carriage of infectious materials through other agents. Emphasis must still be laid on proper sterilization of eating utensils, destruction of all infectious discharges, avoidance of all contamination of foods, and special care being observed regarding the washing of the hands every time the sick are handled.

## TUBERCULOSIS

**Attenuation of Human, Bovine and Avian Tubercle Bacilli.** The object of this short paper by Nathan Raw<sup>2</sup> is to demonstrate the effect of long continued and regular subculturing of pure cultures of human, bovine and avian tubercle bacilli on artificial media containing glycerine. This process has been continued without interruption for twelve years, and the cultivations are luxuriant and grow as readily as in the first year of subculturing. They retain all their characteristic and selective appearances, and can be easily identified as distinct types of tubercle bacilli.

Inoculation of rabbits and guinea-pigs by human and bovine bacilli have been made at intervals during the last twelve years, with the result that there has been a gradual decrease in virulence, until at the present time they are almost non-pathogenic to animals. The source of each of these strains of tubercle bacilli is given. The important factor the author wishes to bring out in the study of tuberculosis is that the human body is attacked by two distinct types of bacilli, namely, human and bovine. Those two types of bacilli can not grow in the body at the same time. Their method of infection is different and selective. Human and bovine bacilli are antagonistic to each other, and a mild infection of one type in the human body will produce an immunity to the other type.

The great bulk of tuberculosis is caused by human bacilli, directly infecting the lungs and setting up primary pulmonary tuberculosis, pleurisy, tuberculous pleurisy, tuberculous laryngitis and secondarily tuber-

(2) Lancet, March 18, 1919.

culous enteritis. As a general rule these infections are limited to the respiratory organs and intestines, and in progressive cases death results from exhaustion and toxemia.

Bovine bacilli are generally conveyed to the body in tuberculous filth and food and infect the various organs through the lymphatic channels. These infections are, as a rule, limited to children and to early adult life. The lesions usually produced are primary abdominal tuberculosis (*tabes mesenterica*), tuberculous glands, tuberculosis of bones and joints, meningitis and lupus, tonsils and adenoids (occasionally), and miliary tuberculosis.

A person with primary pulmonary tuberculosis is not likely to develop a tuberculous bone or joint, and a primary bovine infection is not likely to develop a primary tuberculosis of the lungs. The lungs are, however, not infrequently infected in the course of the bovine infection of other organs. Tubercle bacilli of bovine type would seem to be encountered in from 10 to 30 per cent. of samples of milk submitted to bacteriologic examination, according to Delepine. If the milk is not boiled or sterilized, there is ample opportunity for the infection of susceptible children. The organisms (human and bovine), are not transmutable and can not by any artificial growth be changed from one to the other type.

The real object of the present work was to find out if it was possible to reduce the virulence of the bacilli to such a degree that it might be possible to use them therapeutically in the treatment of active tuberculosis. The longest period before recorded of the attenuation of these bacilli was three years, and that was found to be not enough.

In 1914, several animals were inoculated with the bacilli discussed here, which at that time had undergone nine years attenuation, and the results obtained were practically negative. In no case was any progressive tuberculous process set up in the animals and postmortem examination showed no active tuberculosis. Eight patients with apparently hopeless tuberculosis of the glands, bones and joints, and with lupus, all with discharging sinuses, were treated with inje-



tions of living bacilli at intervals of one week. The injections were made subcutaneously in the triceps region, and beyond redness and slight swelling, no bad effects were observed and the patients noticed nothing unusual. Later, four cases of acute and active tuberculosis with large numbers of bacilli in the sputum were treated in the same way, and just previous to the time of writing this paper, the author examined a hospital nurse, who was treated five years before, and who is now on full duty, and quite cured. All the patients treated in this way are still living, so far as the author knows. All of the cases were treated by mixed bacilli, the cultures being raised to a temperature of 220° F. for two minutes before injection.

Raw points out that the whole object in attempting to cure tuberculosis, is to prevent the growth of the bacilli in the body, and it is felt that this clearly can be done only by some specific method as described in this paper. Cases treated and recorded here are too few, and the time which has elapsed is too short for any definite and final conclusions to be reached, but he is encouraged to think that the careful use of such attenuated bacilli may have the effect of controlling and probably preventing tuberculous infections in the human body in much the same way as vaccination protects against smallpox and antityphoid vaccine against typhoid fever.

**Conjugal Tuberculosis.** The frequency of tuberculosis in the husbands of tuberculous wives, and the wives of tuberculous husbands, compared with the rest of the community, induced E. Ward,<sup>3</sup> to make a further investigation of this fact.

His work includes the study of 4,000 cases of contacts, and his experience leads him to believe that the authoritative view is wrong, that it is direct infection and not predisposition which is the most important factor in the spread of tuberculosis, and that infection is correspondingly more frequent in a case of man and wife, where the exposure to it is greater and more prolonged.

Out of 156 cases in which the mate of a tuberculous husband or wife was examined, ninety-one were found

---

(3) Lancet, Oct. 4, 1919.



to be tuberculous, sixteen suspect, and forty-nine negative; if we reduce these figures to percentage it gives approximately 58 per cent. tuberculous, 19 per cent suspect and 32 per cent negative. Considering solely wives whose husbands were first affected, it was found that of 120 cases, sixty-six were tuberculous, twelve suspect, and forty-two negative; or 55 per cent., 10 per cent. and 35 per cent. While among husbands of tuberculous wives in thirty-six cases, twenty-five were tuberculous, four suspect, and seven negative; or 69 per cent, 11 per cent. and 20 per cent.

Basing his opinion upon these figures, Ward takes the view that a great majority of the mates of tuberculous husbands or wives sooner or later show signs or develop symptoms of tuberculosis. He also believes that the majority of those infected recover, and make a speedier recovery than most tuberculous patients. This may reasonably be attributed to an enhanced immunity conferred by the graduated doses of bacilli which they usually receive.

The author makes no claims that the present contribution is a final settlement of the question, but is sure that this important subject should be reconsidered in the light of the greatly increased material now available.

**The Organisms of Secondary Infection in Pulmonary Tuberculosis.** This investigation deals chiefly with pneumococci and streptococci in this rôle. The work was done by H. J. Corper, W. G. Donald and H. W. Antz,<sup>4</sup> in the Laboratory of the United States Army General Hospital No. 16.

The discussion of "mixed" or secondary infection dates back almost to the time of the discovery of the tubercle bacillus by Koch, and has finally resolved itself into three distinct schools originating from the different views held concerning the significance of such infection.

As defined by these authors, the first of the schools referred to hold that the lesions and more severe symptoms of pulmonary tuberculosis are always and only the result of mixed infection; a belief in the etiologic duality of the disease, held by the Koch school.

Second, the lesions and symptoms in pulmonary tu-

---

(4) Jour. Infect. Dis., May, 1919.

berculosis may be caused by the tubercle bacillus alone, but infrequently secondary organisms may contribute to the more severe symptoms or may be largely responsible for the unfavorable progress of the disease.

The third contention is that mixed infection exerts no influence on the true tuberculous process. It is noted that to establish any criterion, the true significance of secondary infection in those organs or body cavities which have direct access to the air is admittedly exceedingly difficult.

Clinical importance immediately attaches itself to those bacteria found in the blood-stream or in viscera, having no direct communication with the air.

In the present work, the sputum and blood of 216 patients with pulmonary tuberculosis were examined: 104 of these were incipient cases, seventy-six moderately advanced and thirty-six far advanced.

The examination of the blood of 216 cases of pulmonary tuberculosis, using for this purpose both liquid and solid mediums, aërobic and anaërobic, resulted in growth of bacteria in broth only, not in solid mediums, in seven of the cases, four of which gave staphylococcus, a possible skin contaminator, one a moderately advanced case, *Micrococcus tetragenous*, and two far-advanced cases, gave one pneumococcus Type II, and one pneumococcus Type IV and *Streptococcus saprophyticus*. Eight of the 216 patients died within a month after such examination, revealing ulcerated pulmonary tuberculosis, and only one of these gave a positive culture after death (Type II pneumococcus in blood and lungs), whereas blood culture one week before death was negative.

Another case in which blood culture was positive three weeks before death was negative postmortem.

Sputum cultures were made coincidently with blood examinations to correlate the results revealed in the majority of cases—pneumococci and streptococci. The most common pathogenic varieties were pneumococci Types I and III, and *Streptococcus viridans*. A few pneumococci—Type I—and hemolytic streptococci were found. Approximately 30 per cent of the sputums revealed pathogenic pneumococci and streptococci. No practical differences were noted in the percentage of

pathogenic pneumococci and streptococci found when the cases were classified according to open or closed tuberculosis, with or without fever, and with or without râles.

**The Complement-Fixation Test in the Diagnosis of Tuberculosis.** A further effort at determining the value of complement-fixation in the diagnosis of tuberculosis has been made by Henry F. Stoll and Lester Neuman.<sup>5</sup> In this work the test was made in over 100 cases that were referred to the tuberculosis section of the Medical Service in the Walter Reed General Hospital for known or suspected tuberculosis. A few patients were seen only once, the others were examined several times and most of them were in the wards for varying periods of observation. All patients about whom there was any question as to diagnosis were examined by two or more qualified medical officers and with very few exceptions, the stereoroentgenograms were taken after the examination was made. A stereoscope in the ward made possible an intimate study of the patient and his roentgenogram.

Depending on the symptoms, the physical signs and roentgenoscopic findings, the cases were classified into six groups as follows:

I. Signs of small healed lesions present (usually apical): Tubercle bacilli not demonstrated (*a*) symptoms absent or due to some other cause, and (*b*) symptoms suggestive but inconclusive.

II. Small lesions; signs suggesting activity: Symptoms definite (tubercle bacilli may or may not be present).

III. (*a*) Large lesion: parts of one or more lobes involved; symptoms few or absent (*b*) same lesion as in III *a*, by symptoms of activity. Prognosis for arrest, good.

IV. Extensive lesions and complications. Prognosis poor.

V. Possibly tuberculous: (*a*) inconclusive signs, suspicious symptoms, and (*b*) signs of small healed lesions; symptoms suggestive but inconclusive (Group I *a*).

VI. Non-tuberculous cases.

---

(5) Jour. Amer. Med. Ass'n, April 12, 1919.

A summary of this work shows that forty robust men of the surgical service all gave negative fixation tests.

Sixty-eight individuals, when first seen, presented some symptoms, or physical signs, suggesting tuberculosis, yet were ultimately diagnosed as not clinical tuberculosis. The tuberculosis fixation test was negative in 92 per cent. of this group. Of the nineteen patients about whom a reasonable doubt existed and who were classified as "possibly tuberculous" 15 per cent. gave a positive reaction. Of eight incipient cases, 37 per cent. gave positive reactions. Four with moderately advanced lesion, yet few or no symptoms, gave 50 per cent. positive. Of seventeen patients with moderately advanced disease and definite symptoms of activity, but in whom the prognosis seemed good, 65 per cent. were positive. Of eleven with advanced disease and a poor prognosis, 64 per cent. were positive. Of twenty-seven active cases with tubercle bacilli in the sputum, 67 per cent. were positive. Of nine active cases without tubercle bacilli in the sputum, 33 per cent. were positive.

It is at once apparent that the practical utility of the complement-fixation test in the diagnosis of tuberculosis is limited by the fact that the highest percentage of results is obtained in the cases in which its need is least felt, namely, the obvious cases with tubercle bacilli in the sputum.

Nevertheless, from their experience, it seems to these workers that with suspicious symptoms and suggestive yet inconclusive signs, a negative fixation test increases to a considerable degree the probability of the non-tuberculous nature of a given case. With the same symptoms and signs, a persistently positive reaction probably signifies an active tuberculosis. A positive reaction occurring with neither symptoms nor signs does not justify a diagnosis of active tuberculosis, though it is quite probable that there has been an active process recently. In such a case, roentgenoscopy should be employed and the patient observed for several months. With frank signs and symptoms, yet with no tubercle bacilli in the sputum, a negative test can not outweigh the clinical evidence, though in all such cases a Wassermann test

should be made. The diagnosis of tuberculosis is many times one of great difficulty. A careful history, a thorough examination, repeated sputum examinations and roentgenoscopic studies are all of recognized importance and can not be replaced by any complement test yet devised.

**The Complement-Deviation Method in the Diagnosis of Tuberculosis.** A report on the diagnosis of tuberculosis by the complement deviation method, is made by Chung Yik Wang and James Crocket.<sup>6</sup>

It includes a complete description of the technique carried out, the materials used, and interpretation of results. It is sufficient here to give a summary of the results obtained.

The investigation deals with the examination of the serums from 104 tuberculous subjects and 220 controls. Of the tuberculous, in fifty-seven cases tubercle bacilli were found in the sputum, and in forty-seven they were absent. Altogether, forty-nine of the patients had received tuberculin treatment at one time or another in the disease. The controls consisted of 100 positive and 100 negative Wassermann serums, and of twenty serums taken from persons clinically known to be free from tuberculosis.

All the positive Wassermann serums which were found to give a positive reaction in the test were further tested with the chloroform differential method, and in every instance the serums after treatment became negative. It may be stated here that this differential test has been applied, besides those cases just mentioned, to thirty specimens made up of luetic and tuberculous serums, and with no exception all the serums remained positive. It is significant to note in the tabulated results that they do not afford evidence of an effect which tuberculin in the small doses as usually administered has in the production of antibodies in the circulating blood as judged by the reaction of the test; nor have the authors observed any relation between the strength of the reaction and the extent and the severity of the disease. Interpreted according to the rules laid down in this work, arbitrary though they are, the results yielded are expressed as follows:

(6) Brit. Med. Jour., July 5, 1919.



Results	Tuberculous	Controls
Strong positive (+++).....	44	...
Moderately strong positive (++)....	23	...
Weak positive (+).....	22	...
Negative (-) .....	15	220
	<hr/>	
Total .....	104	220
Percentage of positive.....	85	0

The findings in the cases investigated furnish 85 per cent. positives out of 104 tuberculous subjects. As none of the controls examined reacted positively to the test, it may be justifiable to regard the test as specific, and where a reaction is provoked a diagnosis may be safely pronounced, not only that the disease is present, but also that the lesion is in an active condition. Here, as in the Wassermann test, a negative finding is significant though inconclusive.

The authors state that the non-specific reaction which other observers have found was due to the presence of lipoids in the antigen, and in part, also, to the tested serums being insufficiently heated. Even with the delipoidal antigen used in this work, the authors found it necessary, in order to avoid a false reaction, to heat the serum for at least two full hours at 55° C., the usual inactivation for half an hour at this temperature being inadequate for the purpose.

**A New Diagnostic Sign in Incipient Pulmonary Tuberculosis.** The above claim is presented by Jorge Vargas.<sup>7</sup> This sign has been found in 169 cases of incipient pulmonary tuberculosis. It consists of the reinforcement of the whispered voice in the vertex of the affected lung. This sign appears before the disease reveals itself by any other symptom, either auscultatory or percussional, and before respiratory inversion and impairment in the supraspinal triangle of the affected side, which the classics consider as the first sign of the malady to appear. A stethoscope and a little practice are enough to find it. The mechanism of the sign is very simple. It might be said that it is the same as the respiratory inversion, and that examining not the respiratory voice but the whispered voice, the physician

(7) Jour. Amer. Med. Ass'n, Aug. 30, 1919.

resorts to a trick which allows him to confirm the beginning of the tuberculous process, in a period before the appearance of the principal respiratory inversion.

When the peribronchial injury is not sufficiently extensive; when interstitial tissues of the lungs have not yet increased enough to conduct with clearness to the ear that auscultates the tracheobronchial noise, it is sufficient to make the patient repeat in a low voice in each expiration a word rich in consonants. In an instant the ear will perceive the great difference that exists in the case of incipient tuberculosis between the healthy and the affected side. With a stethoscope carefully applied to the ear, isolating outside noises, a very muffled murmur is perceived, at most, from the healthy side, while from the affected side each syllable is distinctly heard, with such force that it sometimes reaches the degree of whispered pectoriloquy.

The author has followed the progress of 169 tuberculous patients from the beginning of the malady; in many of them before the appearance of the slightest symptoms. Always, sooner or later, this sign appeared before the respiratory reinforcement and other signs that, associated, did not leave doubt for the diagnosis.

#### **The Diagnosis of Chronic Pulmonary Tuberculosis.**

This report by Thomas McCrae and Elmer H. Funk,<sup>8</sup> of Philadelphia, is based upon a study of 1200 consecutive admissions to an institution, all the patients coming with a diagnosis of advanced pulmonary tuberculosis.

In the group, seventy-two, or 6 per cent. were found to be non-tuberculous. While there is always a chance of error in clinical diagnosis, there is a check in the necropsy results. There were 134 necropsies in this group, and among these it was found that seven patients had been non-tuberculous, 5.2 per cent., which is fairly close to the previous figure. Of these seven cases which came to necropsy and were found to be non-tuberculous, in five a correct diagnosis had been made by the authors, but two went to necropsy with a diagnosis of tuberculosis in which they were in error. Among these patients the various conditions which were wrongly diagnosed as advanced pulmonary tuberculosis were as follows: cardio-

(8) Jour. Amer. Med. Ass'n, July 19, 1919.

renal, nineteen; pneumonic sequelae, nine; bronchiectasis, eight; abscess of lung, eight; chronic bronchitis, six; neoplasm, five; syphilis, four; aneurysm, two; anthracosis, two; bronchial asthma, two; empyema, two; diabetes mellitus, one; cancer of rectum, one; foreign body, one; malingering, one.

Of the seven among these patients who came to autopsy, the conditions found were abscess, two instances, cardiorenal disease two, and one each of aneurysm, neoplasm, and delayed resolution of lobar pneumonia. Of the two instances in which cases came to necropsy with a diagnosis of tuberculosis, one of the patients had had chronic lung abscess, and the other delayed resolution of a lobar pneumonia.

It is to be understood that there were cases in which these various diseases, with the exception of syphilis and neoplasm, were associated with tuberculosis. There are given only the number of cases in which an error in diagnosis had been made and tuberculosis was not present.

The important question to be considered in connection with this work is: What were the reasons for these errors? In comment on the work the author states that lack of thorough examination, drawing hasty conclusions from symptoms and signs, and neglect of proper sputum examination were probably the main causes. Many of these conditions result in loss of weight and strength with anemia, are accompanied by fever, and show signs in the lungs. The great safeguard is proper examination of the sputum. In any patient with marked signs in the lungs and a sputum negative for tubercle bacilli, suspicion of a diagnosis of pulmonary tuberculosis should be aroused at once. Too often a diagnosis is made and no thought given to proving it. How many negative sputum examinations are necessary before tuberculosis can be excluded is a question that is not always agreed upon. Six negative examinations are said to be enough, but the authors suggest more than this. The problem is very different from that concerned in the diagnosis of early pulmonary tuberculosis. Here one can endeavor to make the diagnosis before bacilli are found in the sputum. In

the advanced form one should never make a diagnosis of tuberculosis unless tubercle bacilli are found.

Of the two instances in which error was made by the authors, one was due to some mistake in the examination of the sputum. A positive result was reported but not confirmed. Either the specimens of sputum or the slides were mixed and a wrong report sent for that patient. There is a rule in the clinic that a positive diagnosis is not to be made on the result of one sputum examination. It must be confirmed. In this case it was not, and that led to error.

To this point in the discussion, mycotic infections have not been mentioned. This has been kept in mind by the authors, however, as the possible source of error, but no instance occurred in this group so far as was discovered. In this connection, one comment may be made on the possibility of finding streptothrix which has come from the mouth. If a careful effort is made to clean the mouth thoroughly, the frequency of the occurrence of streptothrix in the sputum will be found to undergo a striking reduction.

The clinical errors in this group could have been prevented by more care and thoroughness. Some of the mistakes, for example, those in regard to the recognition of syphilis of the lungs or aneurysm are readily made and perhaps not easy to avoid in a case of a man in general practice, but this can not be said of the majority of mistakes. There is little excuse for the error made in the diagnosis of chronic cardiac disease or bronchitis as advanced pulmonary tuberculosis.

A number of the patients considered here had been in tuberculosis sanatoriums and always regarded as tuberculous. This was the case with those patients, particularly, who had bronchiectasis. Some of them stated that a sputum examination had not been made, which is difficult to believe, but it is supported by the fact that an incorrect diagnosis was made. In any institution dealing with patients with chronic disease, it requires constant effort not to rest content with a diagnosis once made. Physicians are too likely to accept the diagnosis of advanced pulmonary tuberculosis as one not requiring special care to make, and when once made not needing re-

vision. How many patients there are today wrongly regarded as having advanced tuberculosis no one can say, but they are not few.

**Early Diagnosis of Tuberculosis.** A Philibert<sup>9</sup> suggests three valuable measures for the detection of latent tuberculosis:

- (1) Exertion test; (2) provoked expectoration; and
- (3) the injection of saline solutions.

In cases in which there is slight or no expectoration the author suggests the administration of a dose of the white oxide of antimony about 0.50 gm. in gum julep. This will increase the secretion and expectoration sufficiently for the search of the tubercle bacilli. In the third test, the patient is kept in bed and the range of temperature determined, and then 50 c.c. of normal saline solution are injected subcutaneously in the morning. Within two hours there is a gradual rise in the temperature curve which reaches its climax about eight hours after the injection, when it begins to decline. The author states that the rise in temperature may at times be as much as three degrees. Following this test, after a suitable period the patient is allowed to take a brisk walk for one hour, and the temperature especially rectal will indicate whether or not there is a rise of temperature.

**The Diagnostic Value of the X-Ray Examination in Pulmonary Tuberculosis.** In this field of work there exists a considerable amount of confusion in the minds of the medical profession because of a lack of skill in interpretation and the expectation that the *x*-ray will tell the whole story unaided. Comparatively few errors are due to overlooking the presence of disease, but many others are made such as diagnosing as tuberculosis a condition which is not tuberculous; however, this feature is not confined to *x*-ray interpretation alone.

In a discussion of the question W. A. Wilkins<sup>1</sup> points out that the first obstacle offered to an easy *x*-ray diagnosis is that nearly all the chests will show some degree of pathology on the *x*-ray plates. This is so constant that it must be accepted as a normal finding. Here

---

(9) Progr. méd., May, 1919.

(1) Canadian Med. Ass'n Jour., April, 1919.



is the pitfall for the inexperienced, a problem for the trained observer and a harvest for the charlatan.

The next difficulty is that the diagnosis is not always worked out in collaboration with clinicians, and even access to valuable information contained in the clinical history sheet may be neglected. It should be emphasized that in order to obtain results, collaboration with the clinician is essential. Special study of the plates may be made of regions which give rise to physical signs: or, on the other hand, an explanation of certain shadows are to be sought for in the physical examination.

The importance of perfect technique for *x*-ray examination of the chest is next emphasized. Wilkins says that good stereoscopic plates in the vertical position are advisable, and the fluoroscopic examination should not be omitted. Information regarding the movements of the diaphragm and of the heart are obtainable only by this method. In a sense, nearly all chests show some degree of pathology, constantly, this condition may be designated as the normal pathology of the chest. This consists of shadows which are seen on the plate of the individual who goes about his daily occupation without the slightest suggestion of any impairment of health. They are also seen in healthy children. These shadows are situated at the root of the lungs, along the course of the bronchi and bronchioles, and at the points of bifurcation wherever branching of the bronchial system occurs. They are cast by the bronchial system with its accompanying lymphatics and blood-vessels, and by the lymphoid elements at the roots of the lungs and at the points of bifurcation of the bronchi and bronchioles. They are normal findings, but their visibility on the plate increases with age and with the extent to which they are involved by pathologic processes. When one considers the impurities that are constantly being inhaled, it is not surprising that the lymphatic system, associated with the respiratory tract, should almost always show some evidence of pathology, but it can not be termed strictly an evidence of disease. Hence, occupation, environment and age, apart from disease, will affect, to some extent, the degree to which these shadows are present.

The quality of the shadow is a matter of extreme im-

portance, varying with the age of the lesion. Old lesions are dense. In recent invasion or in an active lesion the shadow is generally light, feathery, and small in extent, and its favorite situation is in the upper portion of the lung, either supraclavicular or infraclavicular. Another kind of shadow is that which consists of circular, circumscribed and sharply defined shadows which may be found anywhere in the lungs. These merely represent old healed lesions. They are found so frequently that one is forced to the conclusions that in proportion to the number of individuals attacked, tuberculosis, after all, claims the full penalty in comparatively few, and that the majority of cases are light attacks, which run a course unrecognized from invasion to recovery.

Those patients in whom the evidences of tuberculosis are manifested by clinical examination and by the *x-ray*, constitute the greater number of tuberculous cases. The only observation to be made on this group is that the *x-ray* frequently reveals a greater extent of disease than the clinician believes to be present, and that the post-mortem table would probably show greater involvement than indicated by the *x-ray*. Any discrepancy in this group is likely to occur only with reference to the extent of the disease and not with the recognition of its presence.

Another group of patients, that in which the diagnosis is based on the clinical evidence only, should be a small one, in Wilkin's opinion. These cases are the early ones, and situated superficially. The existence of this group and its size will depend upon the determination of what are the earliest clinical signs which will warrant a diagnosis of tuberculosis, and whether or not the pathologic changes are sufficiently marked to cast recognizable shadows on the *x-ray* plates.

A third group of cases comprises those in which the diagnosis is based upon the *x-ray* evidence in the absence of physical signs in the chest. Some clinical evidence of disease is present, such as elevation of temperature, rapid pulse or cough, and the clinician, though suspicious, is unable to locate the site of the lesion by ordinary physical examination. In these cases there are frequently evidences of disease in the lymphoid elements, either at the

roots of the lungs or at some point of bifurcation of the bronchial tree. The author considers that lesions of this nature can be demonstrated by the *x*-ray examination, but to establish the diagnosis requires the support of the clinician.

A fourth group of patients comprises doubtful cases in which a negative opinion has been expressed by both the clinician and the roentgenologist, and in which at a later period a definite diagnosis of tuberculosis is established. In so far as facilities exist for tracing these patients, they form a very small percentage.

**Gastro-intestinal Syndromes Found in Pulmonary Tuberculosis.** The gastro-intestinal symptoms that occur in patients who suffer with pulmonary tuberculosis are discussed from the standpoint of anatomy and physiology by F. M. Pottenger.<sup>3</sup> While the principles put forth in this article have been frequently given out by this author, a brief review will be welcomed by physicians interested in the subject.

It is pointed out that embryologic origin gives to the lung the same double innervation as that possessed by the intestinal tract. All smooth musculature and all secreting glands belonging to the lungs and bronchi are activated, like the stomach and intestines (except the sphincters), by the vagus nerve, which belongs to the parasympathetic division of the vegetative system. Likewise all, except the sphincters, are inhibited by the sympathetics. When the pulmonary structures are inflamed, sensory nerves belonging to both of these systems are irritated and result in reflex action.

Reflexes that affect the gastro-intestinal canal when the lung and bronchi are inflamed, take place through the vagus (parasympathetic). This parasympathetic stimulation is the cause of all the common reflex functional disturbances in the gastro-intestinal canal which result from pulmonary inflammation. When the lung is inflamed the sensory fibers of the pulmonary branches of the vagus are irritated and stimuli are carried to the sensory nucleus of the vagus in the medulla, whence they are transferred to other neurons, with which they mediate, that is, the vegetative fibers of the seventh,

(3) Boston Med. and Surg. Jour., Oct. 23, 1919.

ninth and tenth cranial nerves, and the somatic fibers of the fifth cranial nerves. When mediation takes place with the fifth, seventh and ninth cranial nerves, reflex action results mainly in an increased secretion and an increased irritability of the nasal and oral cavities, the pharynx, salivary and lachrymal glands; in vasomotor disturbance in the cheeks, and tongue; in trophic changes in the tongue, which at times cause it when protruded to turn toward the affected side; and in pain expressed in the sensory neurons of the fifth cranial nerve (head-aches).

Reflex stimulation, if adequate, produces the action which normally belongs to vagus stimulation in these structures—an increased tonus in the muscles and an increased glandular secretion.

The common syndromes on the part of the gastro-intestinal tract which are indicative of a preponderating vagus stimulation and which result from reflex stimuli arising in other organs, which are the seat of inflammation, are nausea, vomiting, hyperchlorhydria, gastric hypermotility, colicky pains, spastic conditions in the intestines, notably spastic constipation, colitis, diarrhea, and intestinal stasis.

The group of functional disturbances makes up a considerable proportion of the symptoms on the part of the gastro-intestinal tract of which patients suffering from early active or chronic semiquiescent tuberculosis complain, and sends the patient to the gastro-enterologist as often, if not more often, than to the specialist in disease of the chest. In fact, the reflex symptoms which are caused by clinical tuberculosis before the advent of marked toxemia, are productive of cough, and during the stage of semiquiescence are practically all expressed reflexly through the vagus in systems other than the lower respiratory; in the larynx as irritation and cough; in the heart as an inhibiting effect producing instability; and in the gastro-intestinal canal in the form of the syndromes before mentioned.

Pottenger says it is a rule that functional disturbances on the part of the stomach and intestinal tract are more commonly an expression of reflex action of some other organ than from the disease of the tube itself. And

when the syndromes here mentioned are present, the appendix, gall-bladder and lungs should be carefully examined for the presence of disease, and eye-strain should be considered.

Colicky pains are known to be very common during the course of pulmonary tuberculosis, and frequently these are due to areas of spasticity in the onward movement of gas. Spastic constipation often results from reflexly increased tonus in the musculature of the colon, the stimulus causing the reflex emanating from the lungs. Also, colitis in tuberculosis has the same reflex basis.

The reflex type of intestinal stasis is caused by a retardation of the intestinal contents in their progress through the canal as the result of spastic conditions in the bowel.

If one substitutes inflammation in the appendix and the sensory fibers of the vagus which supply the appendix in one case, and inflammation of the gall-bladder and the sensory fibers of the vagus which supply it in the other for the inflammation of the pulmonary tissue and the sensory fibers of the vagus which supply it, there could be produced the mechanism which explains the gastro-intestinal symptoms in appendicitis and inflammation of the gall-bladder.

**Active Tuberculosis.** In a discussion of active tuberculosis H. F. Gammons,<sup>4</sup> points out that in order to determine whether a certain case is active or not, one must define activity as it is applied to tuberculous lesions. A tuberculous lesion is said to be active just so long as there is an imperfect or incomplete walling off of the tuberculous focus so that either the bacilli or their poisons can affect the living cells in the vicinity of lesions by continuity, or in distant parts of the body by being carried through the blood-stream.

The author states that in former years he went by stethoscope findings to a great extent, in conjunction, of course, with other signs in determining the activity in any given instance. He laid great stress on the presence of crepitant râles at the apex as denoting activity, as, of course, they do. However, in following these cases month after month and year after year, he found

(4) Boston Med. and Surg. Jour., Jan. 2, 1919.



that apparently the same crepitant râles persisted in the same location, and question has arisen as to the value of finding these râles as a proof of activity. That they mean active pneumonic inflammation is not questioned but the extent of time that they will persist is questionable.

As one compares the other symptoms in similar cases with symptoms in cases in which there are only modified breath sounds, he is impressed with the importance of these other constitutional and toxic symptoms in deciding the activity of a case. Patients are often told by physicians after a chest examination only that the disease is active or arrested without considering other symptoms, such as the pulse and temperature. It is absolutely impossible to say definitely that the case is active by chest examination alone. One can tell that there was activity, but not that it is still present. By examining patients from day to day, the physician may find physical signs differing greatly at various times. But he should not infer that the disease is advancing, as the increase in adventitious signs is probably caused by changes in meteorologic conditions.

It is only by consideration of all factors in the case, that one can arrive at a definite or nearly definite conclusion in regard to the activity of the disease in tuberculous patients. One of the most important signs of activity is elevation of temperature, and of equal importance, is the rapid pulse, especially in beginning cases. Cough and expectoration, loss of weight, appetite and strength, and the tired feeling in the system are indications of active trouble.

Gammons thinks that all tuberculous patients should be tried out on graduated exercise under the supervision of a specialist before final judgment is passed on the probability of the lesion being inactive. This applies only to patients who have no other signs of activity. It is a very frequent occurrence to find individuals who during rest and treatment show no signs of activity, but with a little exercise develop elevation of temperature.

**A Biologic Method for Ascertaining the Presence of Active Foci of Tuberculosis.** In an attempt to ascer-

tain a biologic method of detecting the presence of active tuberculous lesions. H. Wildbolz<sup>5</sup> used the urine of affected individuals and injected it intracutaneously. He found that urine of tuberculous patients when evaporated *in vacuo* to one-tenth its volume and injected subcutaneously caused a circumscribed infiltration of the skin that resembled in form, appearance and disappearance the reactions seen in tuberculin injections. A similar reaction was not found from urines of patients suffering from syphilis or influenza. This would seem to prove, he says, that active tuberculosis anywhere in the body causes a substance allied to tuberculin to be excreted in the urine.

**Pulmonary Tuberculosis Among Soldiers.** A study of pulmonary tuberculosis among soldiers at Camp Cody, New Mexico, is reported by J. F. Studebaker,<sup>6</sup> who summarizes his results as follows:

Of the patients who entered the hospital from September, 1917, to January, 1919, 114 had tuberculosis; seventy-one had served less than six months when considered unfit for active service. Physical strain may either make an acute process more active or reactivate a healed lesion. Family history is of slight value as compared with the previous personal records. Some non-tuberculous respiratory disease most commonly appears in the latter.

Some patients with active tuberculosis may feel perfectly well, not having any symptoms whatever, no cough, no fever, etc. A severe symptom, as hemoptysis, may be the first warning. A widespread involvement of the lung up to this time may exist without the patient's knowledge. The history of cough, loss of strength and weight, afternoon fever, increased pulse-rate and night sweats is of less importance in the early diagnosis, than that of pleurisy, blood spitting, excessive expectoration, and frequent colds, lasting six weeks or longer.

Associated with this, the most significant physical finding is that of localized showers of persistent, moist râles after expiratory cough.

Pulmonary tuberculosis usually takes a general route

(5) Cor.-Bl. f. schweiz. Aerzte, May 31, 1919.

(6) Jour. Amer. Med. Ass'n, April 5, 1919.

from apex or upper lobe downward, and in advanced cases to the opposite side. This should be kept in mind in the differential diagnosis of pulmonary tuberculosis from the influenza sequalae.

**Pulmonary Tuberculosis in Soldiers with Irritable Heart.** In considering the question of a possible relation between pulmonary tuberculosis and the irritable heart of soldiers, John T. King<sup>7</sup> points out that there is a superficial resemblance between the symptoms of these two diseases. Ready fatigue, breathlessness, tendency to excessive sweating, tachycardia and symptoms of asthenia are common to the two conditions. Pain in the left chest, however, which is one of the commonest symptoms of irritable heart, is not characteristic of pulmonary tuberculosis.

In the careful study of men with irritable heart a background of neurotic symptoms, neurologic disease, mental inferiority, emotional instability or psychic maladjustments is almost invariably discovered. Such conditions are, of course, not characteristic of pulmonary tuberculosis. Reference is made to a recent report by Warfield and Smith, who found evidence of pulmonary tuberculosis in a large number of men with the diagnosis of irritable heart or some other synonym of soldiers' heart. In 235 cases of irritable heart pulmonary tuberculosis was found by these authors in eighty-eight patients, or approximately 38 per cent. They are quoted as expressing the opinion that if intensive study had been carried out further, the incidence would have been much larger.

King's investigations were carried out at General Hospital No. 9, Lakewood, N. J., where he studied a group of 246 men with irritable heart of soldiers and found one with definite signs of arrested pulmonary tuberculosis. Two men of the group developed active pulmonary tuberculosis after influenza. No other diagnosis of pulmonary tuberculosis was made.

Intensive study of thirty-two cases of irritable heart showed arrested pulmonary tuberculosis in only one case, with no instance of active tuberculosis.

No evidence was found, from the study of irritable

---

(7) *Archiv. Int. Med.*, August, 1919.

heart at this hospital, that there exists more than an accidental relationship between this condition and pulmonary tuberculosis.

**The Relationship Between Tuberculosis and Disordered Action of the Heart.** This subject is discussed by Captain Horace R. MacIntyre,<sup>8</sup> the basis of the discussion being observations on the subcutaneous tuberculin reaction in 300 unselected cases of disordered action of the heart. In a number of the patients studied, the author was able to demonstrate early apical tuberculosis clinically.

At about this same time another type of case, mostly in youths of from 19 to 21 years, was being studied. These cases were diagnosed as tuberculous mediastinitis and dealt with accordingly.

These two types of case decided MacIntyre to subject a small series of unselected disordered action of the heart cases to both the subcutaneous tuberculin tests and radiographic examination, with a view of determining whether or not he could demonstrate any relation between this condition of the heart and mediastinal glandular enlargement, and a positive tuberculin reaction.

The patients were unselected and were picked at random from those classified as disordered action of the heart under the care of seven different medical officers. Patients who suffered with organic disease of the heart were avoided.

Temperature records were kept for three days to avoid injecting patients who showed an evening temperature of over 99° F. When these were ruled out, the others were given in the subcutaneous tissues old tuberculin equal to 1 mg O. T. Results summarized from the data recovered are as follows:

Positive reactions: 23 (11.5 per cent.); negative reactions, 177 (88.5 per cent.); local reactions only, 70 (35 per cent.).

In discussing what constituted a positive reaction the author says that in keeping with local reactions there were recorded as such only those which showed definite redness and swelling over an area equal to that of a circle 1½ to 2 inches in diameter on the average.

(8) Canadian Med. Ass'n Jour., March, 1919.

The focal reaction gave interesting new information. Precordial pain and vertigo were the most noticeable new complaints. In some instances in which these complaints were elicited before injection, they were complained of as being much more severe following injection.

A few patients complained of palpitation where this had not existed previous to the injection. A noticeable slowing of the pulse rate at rest was also noted. This falling below any previously recorded pulse rate has been established by others as a part of a reaction to sufficient dosage.

General reaction to the tuberculin did not vary from the usual. On the whole, there was looked for a rise of one degree Fahrenheit before declaring a febrile reaction, but in summarizing in the presence of a marked focal reaction in one or two cases the author was able to declare a positive reaction with a rise of less than one degree.

A second group of patients was studied and here they were unselected, and cases of organic disease of the heart were avoided. The same technique and dosage were used as cited above. The results summarized in this group were as follows:

Positive reactions: 9 (9 per cent.); negative reactions: 91 (81 per cent.); local reactions only (not included in positive): 27 (27 per cent.).

In discussing this group MacIntyre states that in disordered action of the heart cases on the whole the local reaction appears to present itself later than in cases seen in a test ward. Of the nine patients who gave a definite positive reaction in this group, seven presented a focal reaction with signs and symptoms referable to the heart and two with a focal reaction gave signs and symptoms referable to the chest.

A summary of these two groups of patients gives the result from a study of 300, as follows:

Positive reactions: 32 (10.6 plus per cent.); negative reactions: 268 (80.3 plus per cent.); local reactions only (not included in positive): 97 (32.3 plus per cent.).

On account of the small single dose of tuberculin used in making these tests, the results may be on the low side throughout. With this technique, it is taken that a



sharp reaction indicates an active tuberculous lesion, and a local reaction is interpreted as meaning a previous healed infection such as is indicated by a positive von Pirquet reaction. Accepting these interpretations as true, it is found that a percentage of unselected cases of disordered action of the heart (10.6 per cent. in this group) have active tuberculosis. Apart from the patients showing active tuberculosis, a still larger percentage (32.3 per cent.) in this group show evidence of a previous and late infection.

Not alone from the cases in which the author has been able to demonstrate clinical tuberculosis, but also from the similarity of the histories of disordered action of the heart patients, to those histories which the author has of patients whom he has seen in civil life at their first appearance at a chest clinic, does he consider that the syndrome known as disordered action of the heart has in the past been more or less recognized as the forerunner of tuberculosis; which disordered action of the heart the poor patient fought against until his cough brought him to a chest clinic.

It is not a little interesting to ponder over the old histories of the chest clinics of civil life, MacIntyre says, and compare them with the histories of disordered action of the heart cases after four years of war. The tales told are the same, but told under entirely different circumstances.

He asks further, how many cases of disordered action of the heart, cause unknown, were early central tuberculosis and were cured by auto-inoculation in the course of their remedial exercise in one or other of the great heart hospitals. Also, would routine tuberculin tests in conjunction with radiography and a well-regulated class, carried out with a view to auto-inoculation of positive cases, increase the efficiency of the service and attach a better prognosis to disordered action of the heart of this type?

**Rest in Treatment of Tuberculosis.** The importance of rest in the treatment of tuberculosis is the subject of an article read before the American Therapeutic Society, June 6, 1919, by F. M. Pottenger.<sup>9</sup>

(9) New York Med. Jour., July 19, 1919.

He states that the healing of tuberculosis resolves itself into first, a process of building up and making the patient strong, and keeping him so for a long period of time, until he becomes master of the invading bacilli; second, a stimulation of the patient's specific defensive powers. The former may be brought about by such measures as open air, suitable food, carefully directed rest and exercise, a healthful mental attitude, hydrotherapy, heliotherapy and such measures as relieve symptoms and complications. The latter may be brought about by products made from the tubercle bacillus or the culture fluid in which it has grown. It is impossible to place a percentage value on any one of these measures. It is also evident that their relative value differs with different patients and under different circumstances.

The disease-fighting power of a patient, Pottenger points out, will depend on his ability to maintain an excess of energy after meeting the natural metabolic requirements of the body. If it requires 20 per cent. more energy to sit in a chair than it does to lie at rest in bed, it is plain that lives can be saved by the conserving force of rest in bed.

Energy is produced by food, not the eating of food but its assimilation. The requirements of food under conditions of rest and various degrees of exercise are about as follows:

Condition	Total Calories
At rest .....	1,750-2,100
Light work .....	2,450-2,800
Moderate work .....	2,800-3,150
Hard work .....	3,150-4,200

In tuberculosis nutrition suffers greatly at times, partly on account of an inability to eat sufficient food, again on account of faulty assimilation. Sometimes the energy output can be readily met when the patient is at rest, but not on exertion. Again, there are times when with large intake and absolute rest, the energy requirements can not be met, except at the expense of the patient's own tissues.

Therefore, the rule for rest, so far as the expenditure of energy is concerned, can be stated thus: The patient

should always rest when exercise will make demands upon his energy output so great that he is unable to meet them fully and still have a surplus for fighting the disease.

Pottenger emphasizes the fact that one can not rely on the disappearance of the common symptoms which accompany tuberculosis as meaning that the disease is no longer active, nor is it necessary that they all be absent before the process is inactive. One must recognize that tuberculosis is a chronic infectious disease in which pathologic changes take place very slowly. The same cycle of changes, from infection to the development of the disease and resolution, which takes place in an ordinary boil in a week, in pneumonia in two or three weeks, in typhoid fever in six or eight days, takes place in tuberculosis in months or years. From the time of implantation of the bacilli with formation of the tubercle in a lung until the time of its producing active tuberculosis or healing may be months or years. Under conditions most favorable for healing, it is the author's opinion that changes continue to take place in the lungs of patients suffering from early clinical tuberculosis for a period of one and one half years. This opinion is based on results obtained from watching contractions which occur in the lung, the data elicited on auscultation, and the time required for the muscles, which are reflexly thrown into spasm by the inflammation in the lung, to lose their rigidity.

What Pottenger considers the ideal technique for applying rest and exercise to the treatment of tuberculosis is outlined as follows:

The patient upon entering a sanatorium is put to bed. If the maximum daily temperature is near or only a degree or so above the normal and there is no other condition to contraindicate it, he is allowed to get up to wash and go to the toilet and to sit up while his bed is being made. Baths, however, are at first given by the nurse. If toxemia, as indicated by fever, or if contraindicating conditions are present, then the wash-bowl is brought to the patient while in bed. If severely ill, the urinal and bedpan are used, and the bed is made without the patient getting up. Patients are treated with this degree of

rest and care until signs of activity lessen, and until such a degree of physical and nervous stability has been reached as to warrant the opinion that increased exercise will be beneficial or at least not harmful.

This long period of rest has been found by the author to be well borne by more than 95 per cent. of the patients. The first few days are the most difficult. Lying in bed relieves certain muscles and brings a strain upon others. These latter ache, just as the muscles which are not accustomed to being used in walking ache after a long tramp. This should be explained to the patient. This discomfort disappears in a few days. The patient needs sympathetic encouragement during this first period, and if properly guided at this time will usually coöperate satisfactorily.

This enforced rest and care is, as a rule, a new idea to the patient. It often impresses on him his first idea of the seriousness of his disease, and thus affords him the reason for whole-hearted necessary coöperation. The few who will not coöperate usually make unsatisfactory patients and obtain unfavorable results. Fortunately, this *régime* is usually quickly followed by improvement and often a very striking one. It shows the patient the value of rest, and if he is intelligent, usually calls forth earnest coöperation.

When the time comes to put the patient on exercise, caution should guide each movement. Pottenger usually allows the patient to sit up only ten minutes on the first day, and then increases five or ten minutes a day according to the particular condition in the patient.

When one half hour is reached, the time of sitting up is divided into two periods, one in the morning and the other in the evening. When one hour is attained, it is repeated for several days, so in two hours, and three before advancing. The length of time taken to advance to two or three hours varies very greatly according to the individual.

When a patient is able to sit up three hours without tiring, he is ready, providing there are no other contraindications, to begin walking. On the first day he walks fifty or one hundred feet, and this is increased by the same amount each day, stopping and repeating for sev-

eral days when a half a mile, one mile and two miles have been attained. The ultimate distance to be reached depends on the patient. So does the rapidity of attaining it. The maximum of some patients will be one-half mile, and that of others ten miles. When possible, the average patient should walk at least two or three miles a day, and the stronger ones five or ten miles before they are discharged from an institution.

It is finally emphasized that the program here outlined is only that for the application of rest and exercise. It alone is not to be considered sufficient. Everything that will aid should be added. Open air, good food, psychotherapy, aërotherapy, heliotherapy, hydrotherapy, tuberculin, attention to symptoms and complications, should each be employed for the 5 or 10 per cent., that it will add to the chances of healing.

**Drugs in Treatment of Tuberculosis.** In this discussion of the place of drugs in the treatment of tuberculosis, the author, Solomon Solis-Cohen,<sup>10</sup> of Philadelphia, confines himself to pulmonary tuberculosis, and to the ordinary slowly developing form, familiarly known as chronic phthisis, although what he says applies in some measure to all forms and varieties of the disease.

He points out the general recognition that drugs occupy a secondary place in the treatment of tuberculosis, and says that unfortunately it has been forgotten that they occupy a necessary place also.

Without proper dietetic and hygienic measures, drugs are of small service. Assuming that the right food is given, that fresh air is provided, that the tissues are kept clean outside and inside by the free use of water, and that rest and exercise are utilized in the right way and at the right time, drugs are of great auxilliary value.

The author considers that his observations have shown the value of three groups of medicinal agencies: iodine compounds, creosote compounds and calcium compounds—to help tuberculous patients to recover and stay well.

Of the iodine group, the best preparation is iodoform, and of this preparation the best is that made by electrolysis. Iodoform is given by preference in the stage of tuberculosis in which there is infiltration before casea-

---

(10) Penn. Med. Jour., October, 1919.



tion and liquefaction have occurred, and it may sometimes be administered with benefit after softening has been checked, but it should not be given while active softening is in progress. Extensive liquid râles, therefore, present a contraindication. The dose is ordinarily  $\frac{1}{8}$  grain weekly or thereabouts until a dose of 1 or 2 grains is reached and then held at that point. Or, if necessary, it may be increased more slowly up to 3 or even 5 grains.

Elementary iodine may be employed in the form of compound tincture, or preferably Lugol's solution, in doses of from 1 to 10 minims in 2 ounces of sugared water after meals.

The use of iodoform internally is usually found satisfactory and the other forms of iodine may be held in reserve for cases in which it is not suitable. The alkaline iodides, however, must be avoided. They are likely to produce softening and certainly hasten it when present.

It is emphasized that in order to be useful the treatment by iodine must be persistent, but that personal reaction varies and must be watched, and the medication increased, diminished or intermitted accordingly.

When liquefaction is in progress, creosote and its compounds, guaiacol and its compounds, or phenol and its compounds, may then be used. Of these, the author prefers creosote carbonate, or creosotal. A fluid dram or more of this preparation may sometimes be given without disturbing the digestion or exciting opposition on the part of the patient. This drug is especially useful when there is any persistent tendency to fever.

Phenol salicylate (salol) may be used when other preparations of creosote or phenol can not be obtained. Because of its phenol constituents, it has been found useful to associate this drug with a lime salt by encapsulating salol and calcium hypophosphate together, usually, from 3 to 5 grains each, one or two capsules being given at a dose three times daily after meals.

Calcium is always used as an auxiliary to iodine or creosote. Calcium lactophosphate is given in doses of from 10 to 15 grains dissolved in a glass of hot water an hour before meals, three times daily, or in soup at meal times. When there is hemoptysis or hemorrhage, calcium

chloride, the crystallized hydrated salt by preference, in doses of 15 grains or more, given every two hours, in solution, and usually with the addition of from  $\frac{1}{8}$  to  $\frac{1}{2}$  grain of codeine, seems to be most prompt in action. The coincident use of dessicated parathyroid gland, about  $\frac{1}{8}$  of a grain to a dose, seems to aid the absorption and utilization of the calcium.

Of other drugs deserving a brief mention, the author places first cod-liver oil, which is to be ranked as a food, a good one, but not always necessary. One of its principals, morrhuol, seems to be a genuine stimulant to the nutritive processes. Either of these is a useful vehicle for creosote in capsules. Arsenic is also of great value as a roborant and metabolic stimulant when such is needed.

Sodium cinamate may be used in doses as large as 5 grains. It may be used at any stage and frequently restrains cough; at first by increasing productivity, later by removing the cause.

Iron and nux vomica may be used to stimulate the digestion or to improve the appetite, or as a so-called tonic. Opiates are not to be dreaded for temporary use, and on distinct indications should be taken advantage of.

**Physical Reconstruction Applied in the Treatment of Pulmonary Tuberculosis.** Reconstruction work as applied to men with tuberculosis is the basis of an article by Frank Billings.<sup>1</sup>

He states that physical reconstruction may be defined as continued treatment, carried to the fullest degree of maximum physical and functional restoration consistent with the nature of the disability of the patient, by the employment of all known measures of modern medical and surgical management, including curative, mental and manual work (in wards, workshops, schools, gardens and fields): physiotherapy (thermotherapy, electrotherapy, hydrotherapy and mechanotherapy, massage, calisthenics, gymnastics, and the like), and sports, games and amusements indoors and outdoors.

The profession, the author says, has found no use for these curative measures, because as a rule physicians and surgeons are satisfied with physical cure. Modern

(1) Jour Amer. Med. Ass'n, Oct. 4, 1919.

medicine and surgery must take heed of functional as well as physical restoration. An interest in the convalescent patient must continue and the physician must prescribe necessary measures in proper doses to insure restoration of functions or to establish it as nearly as the nature of the disability permits. On the other hand, rest, physical and mental, when indicated, even to the most absolute degree practicable, is as much a factor in physical and mental rehabilitation as physiotherapy, curative work or play when these agents are rationally called for.

Tuberculosis is an infection, which, as a rule, is focal in character. The primary focus, usually located in a lymph gland or glands, is acquired usually in childhood. Later in life, the pathogenic agents take on added virulence, or the resistance of the tissues of the host to general or to wider local invasion is diminished or both conditions are present.

Experience has shown that during the acute or active stage of pulmonary tuberculosis, rest as absolute as practicable, is the best method of passive control of the disease. If the patient is fortunate, the active stage abates and in an indefinite time the patient reaches the stage of inactivity of the disease. The reward for such management is marked improvement of the patient's physical disease, but the function of his mind and the circulatory and locomotor organs are far below normal.

Until the blood and lymph circulatory organs function properly, cellular nutrition will remain low. Rationally one can not prolong absolute rest beyond the active or febrile stage.

The second stage of treatment embraces alternating rest and controlled mental and physical exercise. Individual management is indicated throughout the whole treatment program; but in this second stage the dosage of mental or physical exercise prescribed, and the frequency of the repetition must be under watchful medical supervision. If the progress is favorable, the bed rest periods become shorter and less frequent, and conversely the active period in chair and walk become longer and more frequent.

It is during this transition period, between absolute

rest and ambulatory stage, or third period, of treatment, that the wise physician will apply such physiotherapy as hydrotherapy and massage, and occupational therapy modified in kind and dosage to meet the needs of individual patients. Mental and manual occupational therapy should be applied as early as mental and physical activity are permissible.

In addition to what may be termed purely diversional occupations, such as woodcarving and whittling, toy making, bead stringing and block stamping, the patient may take academic courses in English and other languages, including arithmetic, penmanship, and the like. read text-books on and practice stenography, type-writing, Morse telegraphy and radiotelegraphy, book-keeping, banking, etc.

When the patient has reached the ambulatory stage, all the measures embraced under physical reconstruction may be applied with benefit to the tuberculous individual.

Few physicians, Billings says, realize the benefit and the ease and safety of the applications of the alternating hot and cold shower or spray baths. By this means the blood is made to flush the whole body and in consequence aids in washing out toxic waste material, and in the improvement of muscular tone and general nutrition. Pulmonary ventilation is also improved. The end-result is equivalent to considerable active exercise, like gymnastics or walking, without the attendant fatigue of the latter. Likewise, rationally applied massotherapy is recommended.

It is in the ambulatory period that shop and out-of-door pursuits are applicable. The academic and commercial courses may be continued. Controlled recreation in the form of graduated walks, gymnastics, calisthenics, and games indoors and out, has an important place in the treatment of convalescent tuberculous patients.

When the tuberculous soldier has reached the stage of arrest or inactivity of the pulmonary disease he may be discharged from the army.

For the patient with arrested tuberculosis in civilian practice, the conservative physician desires to maintain

and to improve the resistance of the host to the unfriendly parasites by attempting to have the patients follow a rational hygienic life and, if the bank account permits, to spend seasons characterized by inclement weather at resorts where favorable climatic conditions permit them to live comfortably in the open air.

While these measures are correct and rational enough, Billings insists that one should adopt measures of physical reconstruction at this period of convalescence which will so completely rehabilitate the patient that he will be practically immune to further active tuberculous disease.

Physical reconstruction is especially applicable to the patient with arrested or clinically inactive tuberculosis and should have wider application in the final hardening process before the discontinuation of the individual medical supervision.

Concerning the care of tuberculous patients in the army, the author says that from the beginning of the war to Dec. 31, 1918, there were treated in the sanatoriums approximately 8,500 men. During April, 1918, there were approximately 6,000 tuberculous patients in the seventeen military sanatoriums. Of those who took curative work, 2,941 were occupied with the handicrafts and arts, 339 took ward academic instruction in languages and the like, 1,932 received training in commercial and professional subjects; in technical courses including carpentry, shoe repairing, motor mechanics, agriculture, gardening, stock raising, etc., and 725 utilized recreational play in and out of doors. The sum of these figures gives the total enrollment for the month. The total number of patients who took curative work was less than the last figure because some patients were enrolled in two or more curative work occupations.

Finally, it must be recorded that the almost universal testimony of the commanding officers of the hospitals, the ward surgeons, the educational personnel, and the patients is to the effect that curative work in wards, schools, shops, gardens and fields is of the greatest psychologic and material value in the treatment of pulmonary tuberculosis.



## INFLUENZA AND INFLUENZAL PNEUMONIA

**Pneumonic Influenza.** In an introduction to a discussion on pneumonic influenza, Alex Louers,<sup>2</sup> of Melbourne, Australia, suggests first, that the nomenclature of the affection requires immediate amendment. The term "influenza" is said to be derived from an Italian epidemic in the seventeenth century, which was attributed to some malign influence of the stars. It now covers three groups of disorders. The common cold, due to organisms other than the *B. influenzae*; catarrhal fever, with a variety of symptoms; the disease generally attributed to the Pfeiffer bacillus, pandemics occurring at long intervals, such as the one of 1918. The second and third of these classifications have two characteristics in common, namely, suddenness of onset, and the number of persons attacked. Louers suggests that the term influenza should be abolished altogether. If a name must be given to the present pandemic, catarrhal septicemia is a better description, he thinks, of cases associated with hemorrhagic and cyanotic development.

The epidemic being considered is not classified as influenza for the following reasons: First, the Pfeiffer bacillus is frequently not demonstrated. The mortality is much higher than in the infection attributed to the Pfeiffer bacillus. The victims of what has always been called influenza, or catarrhal fever, have been mostly old people. In this epidemic the victims have been largely young adults. There is often a notable absence of the classical nasopharyngeal catarrha signs in many instances, even the most severe.

The next point considered is whether or not the disease gives pneumonia, and to this the author answers "no," because it does not conform to pneumonia, as this disease has hitherto been regarded. A number of reasons are stated in support of this point.

Furthermore, the epidemic is not a new disease, and if one wishes to be convinced of this, all that he must do is to look into the literature and find every symptom that has been observed in the present epidemic recorded by those who observed the previous epidemics.

(2) Med. Jour. Austral., Aug. 30, 1919.

and to improve the resistance of the host to the unfriendly parasites by attempting to have the patients follow a rational hygienic life and, if the bank account permits, to spend seasons characterized by inclement weather at resorts where favorable climatic conditions permit them to live comfortably in the open air.

While these measures are correct and rational enough, Billings insists that one should adopt measures of physical reconstruction at this period of convalescence which will so completely rehabilitate the patient that he will be practically immune to further active tuberculous disease.

Physical reconstruction is especially applicable to the patient with arrested or clinically inactive tuberculosis and should have wider application in the final hardening process before the discontinuation of the individual medical supervision.

Concerning the care of tuberculous patients in the army, the author says that from the beginning of the war to Dec. 31, 1918, there were treated in the sanatoriums approximately 8,500 men. During April, 1918, there were approximately 6,000 tuberculous patients in the seventeen military sanatoriums. Of those who took curative work, 2,941 were occupied with the handicrafts and arts, 339 took ward academic instruction in languages and the like, 1,932 received training in commercial and professional subjects; in technical courses including carpentry, shoe repairing, motor mechanics, agriculture, gardening, stock raising, etc., and 725 utilized recreational play in and out of doors. The sum of these figures gives the total enrollment for the month. The total number of patients who took curative work was less than the last figure because some patients were enrolled in two or more curative work occupations.

Finally, it must be recorded that the almost universal testimony of the commanding officers of the hospitals, the ward surgeons, the educational personnel, and the patients is to the effect that curative work in wards, schools, shops, gardens and fields is of the greatest psychologic and material value in the treatment of pulmonary tuberculosis.

## INFLUENZA AND INFLUENZAL PNEUMONIA

**Pneumonic Influenza.** In an introduction to a discussion on pneumonic influenza, Alex Louers,<sup>2</sup> of Melbourne, Australia, suggests first, that the nomenclature of the affection requires immediate amendment. The term "influenza" is said to be derived from an Italian epidemic in the seventeenth century, which was attributed to some malign influence of the stars. It now covers three groups of disorders. The common cold, due to organisms other than the *B. influenzae*; catarrhal fever, with a variety of symptoms; the disease generally attributed to the Pfeiffer bacillus, pandemics occurring at long intervals, such as the one of 1918. The second and third of these classifications have two characteristics in common, namely, suddenness of onset, and the number of persons attacked. Louers suggests that the term influenza should be abolished altogether. If a name must be given to the present pandemic, catarrhal septicemia is a better description, he thinks, of cases associated with hemorrhagic and cyanotic development.

The epidemic being considered is not classified as influenza for the following reasons: First, the Pfeiffer bacillus is frequently not demonstrated. The mortality is much higher than in the infection attributed to the Pfeiffer bacillus. The victims of what has always been called influenza, or catarrhal fever, have been mostly old people. In this epidemic the victims have been largely young adults. There is often a notable absence of the classical nasopharyngeal catarrha signs in many instances, even the most severe.

The next point considered is whether or not the disease gives pneumonia, and to this the author answers "no," because it does not conform to pneumonia, as this disease has hitherto been regarded. A number of reasons are stated in support of this point.

Furthermore, the epidemic is not a new disease, and if one wishes to be convinced of this, all that he must do is to look into the literature and find every symptom that has been observed in the present epidemic recorded by those who observed the previous epidemics.

(2) Med. Jour. Austral., Aug. 30, 1919.

to one or more of a variety of microörganisms, and most frequently to an association of a coccobacillus with the streptococcus and the pneumococcus. This coccobacillus is similar if not the same as Pfeiffer's organism and has not been cultivated from the blood in the mild cases—pneumococcus type; while the streptococcus seems responsible for the asphyctic form. While the pneumococcus and streptococcus are well able to kill alone, the coccobacillus is so often found in the fatal cases that it must be regarded as a powerful synergist.

Veterinarians know of a number of diseases in animals, especially in horses, which possess points of resemblance to pandemic influenza. Leaving aside contagious pneumonia, we have the affection known as strangles, a protein malady which ordinarily prevails only in the cold months. It is significant that it was very common in the French army horses during the summer of 1918. It has been regarded as due to the streptococcus of Shultz but this is now claimed to cause a secondary infection. Hemocultures shows aërobic coccobacillus which showed a polymorphous suggesting that of the pasteurella, although with cultural differences. The pasteurella can cause a form of hemorrhagic sepsis and often accompanies the *Bacillus mallei* in glanders. It is now stated that the pasteurella in question is found not only in strangles, but in contagious pneumonia. In fact this group of organisms is in evidence in many epizootics and in many ways resemble coccobacillus infection in man. But despite this similarity between human and animal pathology the authors are inclined to the view that pandemic influenza could not occur in the absence of some filtrable virus.

**Microörganisms Resembling Influenza Bacillus as Pus Producers.** Before the recent epidemic, J. L. Burckhardt<sup>5</sup> described a bacillus which differed in no wise from Pfeiffer's bacillus. During the pandemic he was unable to isolate it. The accounts of a pyogenic activator are not lucid in the literature, that is few cases have been shown by experiment to cause pus formation in pure culture. The author reports two cases: one was in a nursling with suppurating joints while the other

(5) Cor.-Bl. f. schweiz. Aerzte, Sept. 11, 1919.

was in an adult with pleurisy. The pus in these cases was free from blood, but in experimental disease in guinea-pigs the germs possessed hemoglobinophilic properties. They were present in pure culture in both cases and produced hemorrhagic lesions when injected.

While in clinical influenza Pfeiffer's bacillus is not found in the blood, in some cases apparently the same organism with hemoglobinophilic properties has been identified in that location even following its first recognition. Thus in 1907, in four fatal cases of bronchopneumonia in infants, Menier found the Pfeiffer organism in the blood, and by inoculation its culture into animals produced septicemia. The question of identity of this germ with the Pfeiffer bacillus must still be left open.

**The Pfeiffer Bacillus in Influenza.** An investigation has been carried out by C. W. Duval and W. H. Harris,<sup>6</sup> to determine the rôle of the Pfeiffer bacillus in the recent epidemic of influenza.

They recall that there are three views existant today regarding the relationship of *B. influenzae* to the epidemic disease: First, the acceptance of Pfeiffer's work and its confirmation by other reliable investigators; second, that the view that the influenza bacillus plays only the rôle of the secondary invader, and that the disease is primarily caused by a filterable virus; third, that the Pfeiffer bacillus, together with other pathogenic microorganisms of the respiratory tract flora, produce conjointly the syndrome called "influenza."

Since the medical press has contained so many conflicting views concerning the etiology of epidemic influenza, and the significance of various bacteria in the respiratory tract, the main dispute being over the part played by the Pfeiffer bacillus, it is considered that the present study of the etiology will not be amiss at this time.

The study is based on numerous cases of influenza in various hospitals in New Orleans, during the primary and secondary outbreaks of the infection. Among the number were included seventy-five Porto Rican sailors ill with the disease, who were selected for study because

(6) Jour. Infect. Dis., November, 1919.



they offered unusual opportunities in that they were all from the same source, and clinically presented the same infection. In this work, cultures were made of the sputum, of the blood and tissues, especially from the lungs in cases in which necropsies were held. Gross and microscopic observations of the lesions found at post-mortem were made, also repeated blood examinations during the course of the infection and serologic study. In conjunction with the work, approximately 5,000 persons were vaccinated with the protein of killed influenza cultures, and the results have some bearing on the etiologic relationship of *B. influenzae*.

In summarizing the results obtained and the conclusions reached by this work, it is said that the micro-organism known as the bacillus of Pfeiffer may be isolated from the material of the respiratory tract lesions in all cases of epidemic influenza and recovered only occasionally from persons not infected.

There is adequate proof that the Pfeiffer bacillus is a member of the normal upper respiratory tract flora. That it may occur in normal individuals during epidemic times, or persist for months in those who have recovered from the infection is well recognized. These persons are the *interim* carriers of the bacillus and constitute an important means for transmission of the infectious agent.

During the course of the infection, and for a variable time after recovery, the blood contains specific immune bodies for *B. influenzae* while those not infected are without these substances.

The subcutaneous inoculation of persons with influenza protein causes the production of specific immune bodies. The reaction occasioned in the inoculated person is definite evidence of its toxic property.

Secondary infections with one or more of the ordinary respiratory tract flora is common in epidemic influenza and is usually responsible for the occurrence of pneumonia.

The Pfeiffer bacillus is the primary cause of epidemic influenza for the reason that sufficient postulates in the recognition of its etiology can be fulfilled.

[This positive statement is contradicted by many other

investigators. Further study and investigation must be carried on before the question of the etiology of pandemic influenza is conclusively settled.—B.]

**The Infecting Agent in Influenza.** The results of an experimental research dealing with the infective agent in influenza are published by T. Yamanouchi, K. Sakakami, and S. Iwashima.<sup>7</sup> They state that during the winter of 1918, influenza caused the loss of many lives in Japan. According to official statistics up to the end of January, 1919, there were nearly 30,000,000 cases, of which 170,000 proved fatal. Inasmuch as fifty-two doctors and nurses offered themselves as subjects for experiment, the authors have been able to solve some important questions relating to this infectious disease. These experiments which are now recorded were made between Dec. 1, 1918, and the end of March, 1919. The experiments are described as follows:

An emulsion of sputum from forty-three influenza patients was made in Ringer's solution. This emulsion was injected into the noses and throats of twelve healthy persons.

A filtrate (by Berkefeld filter) of the same emulsion was injected into the noses and throats of twelve other healthy persons.

The results of these experiments are very significant: Among the subjects treated were six persons who had already had influenza, and all six showed no symptoms of illness. But all the other eighteen subjects, both those who had received the emulsion and those who had received only the filtrate, were attacked by the disease, after an incubation of two or three days. Their fever was sometimes slight ( $37.5^{\circ}\text{C.}$ ), sometimes very severe ( $39^{\circ}\text{C.}$  or more.) The subsequent symptoms were headache, sore throat, lumbago, cough, etc.

A filtrate of blood of influenza patients was injected into the noses and throats of six more healthy persons. The results were precisely the same as in the previous experiments.

Four healthy persons were inoculated subcutaneously with the filtrate of the sputum emulsion and four others with a filtrate of the blood of influenza patients. With

(7) *Lancet*, June 7, 1919.

the exception of one who had previously had influenza, they all developed the disease after two or three days' incubation.

A pure culture of Pfeiffer's bacillus and a mixed preparation of the pure Pfeiffer bacillus, along with pneumococci, streptococci, staphylococci, diplococci, and many other similar microbes common in the sputum of influenza, were injected into the throats and noses of fourteen healthy people, who had not had influenza. There were no symptoms of illness following these injections.

The following summary is given:

The germ of influenza can not be removed by filtering (filterable virus).

The germs can infect through the mucous membrane and also by inoculation.

The germs can be found in the sputum and the blood in influenza patients.

The known bacilli, such as Pfeiffer's bacillus, pneumococci and some diplococci are not the cause of influenza.

"We observed experimentally that all people who have previously had influenza or received the sputum emulsion or its filtrate are immune to the disease."

**The Bacteriology of Epidemic Influenza and Pneumonia.** The object of this study by Ralph A. Kinsella,<sup>8</sup> Major in the U. S. Army, was to determine, if possible by cultural methods, the bacterial agent operating in cases of epidemic influenza and pneumonia.

For this purpose, smears and cultures of the nose and throat in the early stages were examined, blood cultures were made in the cases of pneumonia, the sputum was injected into white mice and, finally, cultures were made at necropsy.

The details of the method are presented fully. In comment upon the results obtained, the author states that they suggest that influenza is a disease caused by some as yet undiscovered agent, which produces inflammation of the entire respiratory tract, and effects a very profound lowering of resistance, which is perhaps expressed by the constant and striking leukopenia. Lack

(8) Jour. Amer. Med. Ass'n, March 8, 1919.

of reaction is the most noticeable clinical feature. Under these circumstances, invasion follows by the various bacteria that are capable of becoming pathogenic, although harmless in the normal mouth.

The various bacteria commonly found in normal throats are encountered in the cultures from influenza patients. The experience of many investigators is that the Pfeiffer bacilli may be pathogenic and cause a form of purulent bronchitis and bronchial pneumonia. This organism occurs with striking frequency in the throats of patients with measles, pertussis, diphtheria and scarlatina, especially when these conditions are complicated by the form of bronchitis or bronchopneumonia mentioned. The Pfeiffer bacillus occurs with frequency in normal throats in times when no epidemic of influenza exists.

**The Bacillus of Spanish Influenza.** A preliminary report of bacteriologic investigation of influenza is made by A. J. Hinkelman and Carol P. Hinkelman.<sup>9</sup>

They have isolated an organism from cases of Spanish influenza that so strikingly meets the requirements of Koch's law of specificity as to throw a new light upon the disease.

The organism is a tiny rod measuring, like Pfeiffer's bacillus, about 0.2 micron in width and about 0.5 micron in length, and in old cultures becomes almost invisible. It is Gram-negative and, like the ordinary influenza bacillus, at times takes the stain more deeply at the poles. Colonies on blood-agar plates appear in about eighteen hours as large, bluish white droplets, with irregular edges, and tending to spread out from the highest elevation and become confluent.

The organism is motile and does not ferment glucose, nor acidulate milk. It is not a recognized fact that Pfeiffer's bacillus has much pathogenicity for the common laboratory animal. The organism in question, however, has its strong point in this respect.

The organism isolated from the sputum of patients suffering from influenza, whether of the mild and severe or the fatal form, has a powerful elective affinity for the respiratory tract of laboratory animals, and in rab-

(9) New York Med. Jour., April 26, 1919.

bits and guinea-pigs, both the living and the dead organism produce the identical symptoms and the same pathology as the authors found in cases of influenza in man, both by way of the respiratory tract and by way of circulation.

The organism may be recovered again from the lesions of the dead animals, and, when injected into a second animal, it produces the same results as the primary inoculations.

In a small proportion of cases of influenza, the organism may be isolated directly from the sputum by ordinary cultural methods. In those cases showing an extensive mixed infection of such secondary invaders as streptococci, pneumococci and *Micrococcus catarrhalis*, the same organism may be isolated by using rabbits or guinea-pigs as a filter.

The specific action of the organism depends upon either an ectotoxine or endotoxine that apparently further depends on some biochemical change in the blood as a result of the action of some unknown product not essential to life, and is not present in the blood of all individuals.

It appears possible to neutralize whatever the fatal base is, for a number of people, especially between certain ages, with blood that does not contain it.

The organism, though of the morphology of Pfeiffer's bacillus, is not the same.

The action of the organism is strikingly specific and does not depend upon such secondary invaders as streptococci, pneumococci and the *Micrococcus catarrhalis* in producing any of the clinical symptoms of influenza or its pathology.

Treatment resolves itself into further study of the true nature of the poison the organism in some way produces or carries with it, and of the biochemical laws of the human blood serum, whereupon apparently depends the fate of the individual in the course of the infection. In the absence of complete understanding of the chemistry of the organism or its poison, the use of a vaccine made from pure cultures should not be encouraged because of the possible danger of elevating the bacteriolytic index of the individual blood serum.



The disease of the recent epidemic is not influenza of the form well known and of past epidemics, and the term Spanish influenza has been used in this article for the express purpose of leading the reader away from the thought of the old time disease and to avoid confusion of this later and more fatal infection with it.

**Transmission of Influenza.** An investigation for the purpose of ascertaining some possible factors in the mode of transmission of influenza through the use of human subjects for experiments has been carried out by H. R. Wahl, G. B. White and H. W. Lyall.<sup>1</sup> Two objectives were sought: First, to determine the infectious nature of bacteria-free filtrates as reported by Nicolle; second, to test the pathogenicity of various typical strains of influenza bacilli in man, and ascertain if their use would result in the production of the disease.

For this work, six apparently normal men, officers assigned to the Yale Army Laboratory School at New Haven, having been fully informed as to the possible hazard, volunteered as subjects to be experimented on in this work.

They were quartered and strictly isolated in the isolation pavillion of the hospital. Two of the volunteers had not been vaccinated with any influenza vaccine, while the others had taken a polyvalent influenza vaccine from four to six weeks previously. One of the two mentioned had had pneumococcus vaccine. None had had influenza. On admission to the hospital, all the men were kept under observation for four or more days before being used. Careful physical, clinical and laboratory examinations were made and recorded during this period. The first experiment carried out was made for the purpose of determining the infectiousness of the filtrate, typical influenza lung, when applied to the nasopharyngeal mucous membrane of man. Two filtrates were prepared and used.

A second experiment consisted in applying various strains of *B. influenzae* to the nasopharyngeal mucous membranes in order to determine their pathogenicity.

A third experiment had for its purpose the deter-

---

(1) Jour. Infect. Dis., November, 1919.

mination of the pathogenicity of the freshly isolated strain of the influenza bacillus from the unconsolidated portion of the lungs in a fatal case of influenza pneumonia in which the influenza bacillus was present in large numbers along with an indifferent streptococcus, staphylococcus of both albus and aureus types, and a Gram-negative bacillus belonging to the Friedlander type.

By these experiments upon volunteers, it was found that the nasal application of a filtrate from pneumonic lungs of an individual dead from typical influenzal bronchopneumonia failed to call forth any abnormal symptoms.

The application to the mucous membrane of the nares and nasopharynx of five healthy men (four inoculated from 4.6 weeks before against influenza with a polyvalent influenza vaccine, one uninoculated) of freshly prepared suspension of four different live strains of *B. influenzae* (one, in the second generation from the fatally infected human host) even in the massive doses, failed to produce any abnormal symptoms.

The implantations of living suspensions of influenza bacilli produced no material alteration besides the addition of the influenza bacillus itself.

When experimentally implanted, the influenza bacillus disappears from the nares in a relatively short time, from 24 to 72 hours.

When experimentally introduced into the nasopharynx of man, the influenza bacillus exists and multiplies for a considerable length of time, two weeks or more, and apparently shows considerable resistance to the action of dichloramine-T.

In the examination of the nasopharyngeal secretions of patients suffering from infections diagnosed clinically as typical influenza, and in tissues of the respiratory tract of patients who died of influenzal bronchopneumonia, it was found that the oleate plates frequently gave positive results when the blood and chocolate plates were negative and, in addition, by inhibiting the growth of streptococci and pneumococci, greatly facilitated the isolation of the influenza bacillus. In every case the chocolate plate gave more information than the blood

plate which was used only in picking pneumococci and making a hasty diagnosis of the type of streptococcus present.

It is recommended that in the routine bacteriologic examinations of all suspected influenza cases, plain, infusion, chocolate and oleate or soap agar be used. The blood plate should not be discarded, because it gives information regarding the presence or absence of streptococci, and pneumococci that are liable to be missed otherwise and that may play a not unimportant part either in a symbiotic rôle or as a complicating factor.

**Nature and Modes of Action of the Pathogenic Agent in Influenza.** B. Roussy<sup>2</sup> observes that while every one today agrees that influenza is contagious, there is wide divergence as to the primary cause. In general, microbes—pneumococcus, streptococcus, staphylococcus, pneumobacillus—are looked on simply as agents of secondary infections. Among those described as primary causes, the Pfeiffer bacillus is spoken of particularly, though many authors include it also in the first category.

It is generally asserted that the influenza virus is contained in the secretions of the respiratory passages, and is thence transported by the hands, or various objects, to the conjunctivae or the upper air passages of healthy individuals. Again it is claimed, almost as demonstrated, that contagion occurs by dried sputum, or fluid drops expelled during speech, coughing, etc. Roussy believes this last mode of contagion must be exceptional and accidental. He asserts that it is not possible for an influenza patient to discharge a cloud of fine drops which last long enough to float in the air, the droplets of rain, which are finer, fall rapidly. He suspects a more general mode of contagion—by infectious air. As a result of some observations (1894), he declares that one attack of influenza so far from conferring resistance against a subsequent attack on the contrary renders one more susceptible. On breathing, for a few minutes, the air confined in the room of a patient with influenza, he has many times felt "without doubt, the first manifestations of the contagion." Being convinced that influenza develops without incubation, he compares the mode of action of the virus to some volatile substance, and connects his

observations with the recent researches (Nicolle and others), which go to prove the influenzal virus is filtrable. In short, the warm expired air passing over the layer of secretions on the air passages becomes charged with watery vapor and germs. If we struggle against the free secretions emitted during talking, coughing, etc., the air which surrounds the patients should also be regarded as suspicious.

### **The Influenza Bacillus in Paranasal Sinus Infections.**

Because of the difference in opinion as to the nature of the organism responsible for the influenza epidemic of 1918-19, the following work was done by S. J. Vrowe and W. S. Tracker-Neville,<sup>1</sup> of Baltimore. The object of their study was to determine whether or not Pfeiffer's bacillus occurred more frequently in a series of infected nasal sinuses observed immediately following the epidemic than in a series of such cases observed during a period when there was no epidemic. Consequently within six weeks after the epidemic had subsided a careful bacteriologic study of every case of sinus infection treated at the Johns Hopkins Hospital was made.

For comparison, the authors collected the results obtained by culturing similar material during the periods from 1912 to 1918. A complete bacteriologic study had been made on seventy cases during this time and the influenza bacillus was found in the antrum in fifteen cases or 21 per cent. The streptococcus was found in thirty-three cases, 47 per cent; in ten of these the organism was hemolytic. Pneumococcus occurred twelve times, 17 per cent. Staphylococcus was found in sixteen cases or 22 per cent; in one of these it was hemolytic. The *Bacillus proteus* was found once and the diphtheria bacillus twice.

In a second group of patients studied, there were thirty observed during the three months immediately following the subsidence of the influenza epidemic, and the influenza bacillus was found in the antrum in eight of these patients or 26 per cent. The streptococcus was again the predominating organism (fourteen cases of 46 per cent.); of these fourteen cases in four it was hemolytic. The following organisms were occasionally

---

(1) Bull. Johns Hopkins Hosp., November, 1919.

found: the hemolytic streptococcus in four cases, the pneumococcus in three cases, the *Micrococcus catarrhalis* in two cases, and a Gram-negative diphtheroid bacillus in three cases. The diphtheria bacillus was found in one case, the *Bacillus lactis aërogenes* once, and the *B. proteus vulgaris* in two cases.

The influenza bacillus was recovered from the antrum in pure culture in four instances during this study.

From these results, it is easy to see what the authors infer, that the influenza bacillus like the streptococcus and pneumococcus is a secondary invader and not the primary cause of the disease known as influenza.

**Occurrence of *Bacillus Influenzae* in the Normal Throat.** This study of the occurrence of *Bacillus influenzae* in the normal throat by Agnes I. Winchell and E. G. Stillman,<sup>2</sup> is a continuation of the work of Pritchett and Stillman on the occurrence of *Bacillus influenzae* in throats and saliva with additional observations upon the media used and a study of the distribution of this bacillus among the personnel of two institutions.

Pritchett and Stillman found that of 177 persons who gave no history of having influenza, seventy-four, or 42 per cent., harbored *B. influenzae* in their throats during November and December of 1918. The total incidence of influenza bacillus carriers among 231 normal and late convalescent individuals was ninety-nine, or 43 per cent. From forty-nine cases of uncomplicated influenza, *B. influenzae* was recovered in forty-one instances, or 83 per cent., while from 43 cases complicated by bronchopneumonia this organism was cultivated in forty, or 93 per cent. Of six cases of bronchopneumonia, which were probably late cases of influenza, all showed influenza bacilli. The incidence of *B. influenzae* was much lower in twenty cases of lobar pneumonia, as only eleven cases, or 55 per cent., were positive.

In the present work as in a previous study, the medium used for the isolation of *Bacillus influenzae* was Avery's oleate hemoglobin agar.

Cultures were taken once a month for a period of six

<sup>(2)</sup> Jour. Exper. Med., November, 1919.



months from the throats of the personnel of the Laboratories and the Hospital of The Rockefeller Institute.

The results obtained in this work are tabulated and the conclusions reached from the results are brought out clearly in the discussion where it is said that whatever may be the etiologic relationship of *Bacillus influenzae* to epidemic influenza, there is little doubt of the significance of this organism as a secondary invader in this type of respiratory infection. Facts, therefore, concerning the distribution, occurrence, and persistence of *Bacillus influenzae* in the secretions of the respiratory tract are of importance in epidemiologic investigation and in prophylaxis.

In the study of the occurrence of *Bacillus influenzae* in throats and saliva during the epidemic of influenza last fall, Pritchett and Stillman found this organism present in 42 per cent. of 177 healthy persons from whom no history of respiratory infections was obtainable. These observers found the same organism in the throats of convalescents from influenza in 46 per cent. of individuals studied.

In the same epidemic period, Lord, Scott, and Nye, by cultural methods, demonstrated influenza bacilli to be present in the pharyngeal secretions of 76 per cent. of thirty-four healthy men of the Harvard Student Army Training Corps. Opie and his collaborators, by cultural and mouse inoculation methods, found *Bacillus influenzae* in the mouths of 35.1 per cent. of all healthy men examined at Camp Funston. These figures serve to indicate the wide distribution and prevalence of the organism during the severe epidemic of this acute respiratory disease.

Since the group of individuals studied by Pritchett and Stillman comprised for the most part the personnel of The Rockefeller Institute, it has been possible to make repeated cultural examinations of the throats of eighty-four of the same persons during the six months subsequent to the original observation.

The present study indicates that the percentage incidence of those harboring *Bacillus influenzae* in the upper respiratory tract is as great during the post-epidemic period as it was during the influenza epidemic.

From December 1918, to June, 1919, the percentage of carriers in a group of 150 individuals has been found to average 41 per cent a month. In a boys' orphan asylum in which no case of influenza had occurred during the epidemic, 39 per cent. of throat cultures taken from 190 boys showed the presence of *Bacillus influenzae*. This percentage incidence of positive cultures was the same as that found in the examination of fifty-two convalescent influenza patients in an institution for girls in which over half the personnel had suffered from the disease.

The present study indicates and demonstrates that in the absence of a focus of infection *Bacillus influenzae* may dwell on apparently normal mucous membrane for long intervals.

**Serum Studies on Etiology of Influenza.** The main purpose of this investigation which was carried out by John A. Kolmer, Mary E. Trist and Elizabeth Yagel<sup>3</sup> was to determine whether antibodies for *B. influenzae* occur normally in the serum and the degree and kind of antibody production for this bacillus during influenza.

Similar studies were made with streptococci, *M. catarrhalis*, staphylococci and other organisms isolated from persons suffering from or succumbing to influenza, on the basis that such immunologic examinations may show in a broad and general manner which of these organisms had assumed sufficient pathogenicity in Philadelphia to stimulate antibody production.

The serums of nine healthy adults varying in age from 20 to 32 years, who had escaped influenza and had not received any vaccine, and the serums of thirty-one adults in varying stages of influenza were tested for the presence of thermostabile opsonin, agglutinin and complement-fixing antibody with various bacterial antigens; comparison is made of the results obtained with serums of healthy persons and with those obtained in varying stages of influenza inasmuch as opportunity was not afforded for the examination of the serums of persons prior to their illness or at intervals during the attack of the disease.

Methods used in this work are fully described and the

---

<sup>3</sup> Jour. Infect. Dis., June, 1919.

results obtained are accurately tabulated. The authors state that the general results indicate that antibodies and particularly the complement-fixing body, are developed in the serums of most influenza patients for *B. influenzae* and to a lesser extent for hemolytic streptococci and *M. catarrhalis*; similar studies were not made with pneumococci. These results, however, can not be interpreted as an indication that the bacillus of influenza is the primary or chief cause of influenza inasmuch as this bacillus very probably possesses in the majority of cases sufficient pathogenicity to stimulate antibody production as an organism of secondary infection. Similar studies with the streptococci of scarlet fever and the micrococci of acute anterior poliomyelitis indicate that what are very probably organisms of secondary infection, may stimulate specific antibody production.

In general, the results of this investigation indicate, on the basis of antibody production by the various organisms studied, that the bacillus of influenza produces most antibody during the course of the disease, and if this bacillus is not the actual or primary cause of the infection it is at least the chief organism of secondary infection, with streptococci ranking second in antibody production and importance.

**The Filter-Passing Virus of Influenza.** A final report of an investigation of the cause of influenza, reported first in the *British Medical Journal*, is published by John Rose Bradford, E. F. Bashford and J. A. Wilson.<sup>3</sup>

The essential features of the work are set forth in the preliminary report, but certain features are elaborated in the present article.

The epidemic, which was seen among soldiers where this work was carried out, and the various complications of the disease, are carefully described, also the cultural methods used are outlined, as well as animal experiments and their results.

The authors state that the experiments described show all the lesions of influenza have been reproduced in animals by the injection of pure culture of an organism isolated from man, and fulfill all the requirements nec-

---

(3) Quart. Jour. Med., April, 1919.

essary to establish that organism as the cause of the disease. They consider it important that the disease was reproduced in the first place in attenuated form as in polyneuritis. The increase in virulence by passage so that, for example, the mortality in subdural inoculations rose from a probable four in six to a real mortality of three in three and perhaps the fatal effects produced in all pigs re-inoculated for the third time, may have a bearing on the greater severity of late phases of the epidemic during which this work was done. The success of subdural inoculation and the rapidity of onset thereafter may give support to the opinion that the organism finds entrance to the body by way of the nasopharynx, but does not exclude other means of entrance to the body than by way of the nasopharynx. The numerous sites in which the organism is found in the body, and its presence in the bile and kidney and also in the urine of monkeys, shows that the nasopharyngeal mucus is not the only channel of its excretion. The prolonged residence of the organism in the tissues may likewise be of epidemiologic significance in the production of strains of heightened virulence.

The only explanation of the rapid constitutional and widespread tissue effects following subdural inoculation is that it speedily passes to the blood, producing primarily a septicemia, and thereafter an extensive destruction of minute vessels with many secondary consequences. The whole of the finely coördinated mechanism which in health ensures both a uniform distribution of blood and of air throughout the vascular and air tubes of the lung is disorganized in acute cases within twenty-four hours.

The grave state of the lesions at the margins and bases of the lungs is probably not the direct action of the virus or its products, but largely mechanical. The dead inelastic but porous tissue in a still expanding thorax occurs at the sites where the respiratory movement of the lung is greatest, and this factor largely determines the greater filling of the alveoli and tissues generally with blood and transuded fluid oedema at the margins and bases of the lungs. It becomes also a matter for consideration in how far this mechanical factor,

combined with the disorganization of the physiology of respiration, determines the early gravity of the lung lesions as a whole, to the exclusion of a specific action on the capillary endothelium.

While there is evidence that the effects occur more rapidly and severely in the lung than in other organs,

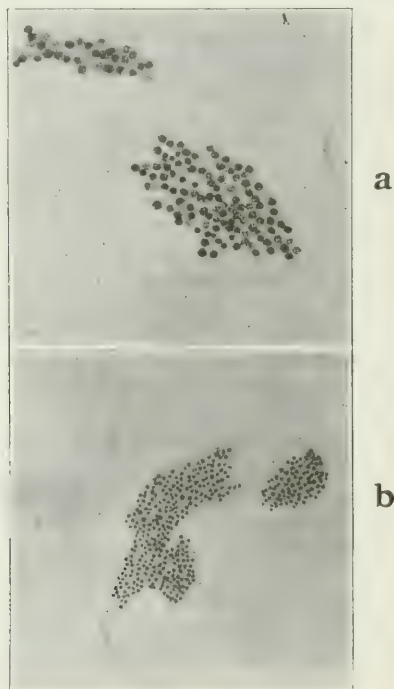


Fig. 2. Culture from Sputum.  
5 days' growth.

(a)  $\frac{1}{16}$ -in. obj. Baker.

(b)  $\frac{1}{12}$ -in. obj. Angus.

there are departures from this general rule, and it has been possible by experimental means to obtain partial, indeed very good, exemption of the lung. Influenza should no longer be regarded as primarily a disease of the lung. The process is exactly the reverse. The lung is not attacked through the air passages by a gradual



extension downward from the higher respiratory passages to the alveoli. The lungs are attacked from within the body throughout their entire vascular mechanism from the blood-stream, in company with other organs in varying degree. Masses of dead or disorganized tissue and blood-clot and the disorganization of respiration soon provide not only foci for local secondary infective processes, but also means by which the secondary infections in their turn, come to produce septicemia on their own account by a reversal of the process in an individual weakened by the primary disease.

The bacteriologic investigation in this work was carried out by J. A. Wilson. It had for its primary object an attempt to demonstrate the presence of a filterable virus in the blood of cases of influenza by cultural and experimental methods. Successful in this attempt, the scope of the inquiry was widened to include the examination of the sputum and other material which might be available from the complications of the disease. In all, sixty cases were investigated, and the specimens examined in connection with them are stated in the following table:

A. Blood, sputum and pleural fluid in.....	4 cases
B. Blood and sputum .....	9 cases
C. Blood only .....	11 cases
D. Sputum and pleural fluid.....	8 cases
E. Sputum only .....	19 cases
F. Pleural fluid only.....	4 cases
G. Blood and urine.....	1 case
H. Blood and postmortem tissues.....	1 case
I. Cerebrospinal fluid and postmortem tissues.	1 case
J. Postmortem tissues .....	2 cases

The results accomplished by this bacteriologic work are set forth in the following summary:

An organism, of definite morphologic and cultural characters has been isolated from cases of influenza.

It can be demonstrated in the blood, sputum and other exudates, and in the tissues, postmortem, by appropriate methods of staining.

It belongs to the group of "filter-passers" a group of organisms which pass through bacteriological filters.

It has been seen microscopically in the filtrate and

has been cultivated therefrom. It has not been found in a large series of controls.

The conditions produced in animals by the injection of these organisms into them are shown in extensive colored plates. One of these showing the changes produced in the kidney is included here. Also the organism as seen in culture is represented in the accompanying illustration (Fig. 2).

**Research into Etiology of Influenza.** The present report is merely a summary of the work done to the date of the writing of this article by H. Grame Gibson, F. B. Bowman and J. I. Connor,<sup>4</sup> and the work is presented in as concentrated form as possible. It consisted of animal inoculation and cultural experiment with filterable virus. The work is divided into four parts.

Inoculation of animals with sputum from cases of influenza.

Inoculation of animals with blood from cases of influenza.

Passage of the virus from animal to animal.

Cultural experiments and inoculation of cultures into animals.

The detail of this experimental work as presented by the author does not permit of an abstract of any greater value than their own summary, presented at the end of the article. The number of experiments carried out is too small to warrant formulating final conclusions. The experiments were brought to an end by a cessation of the epidemic and the loss of laboratory attendants consequent to demobilization. The authors feel, however, that they are in a position to make the following deductions from their work:

1. The apparent immunity of some animals to filter-passing virus and the occasional difficulty of the transmission of these viruses by means of blood is well known. When this is taken into account the number of positive results obtained would seem to be significant.

2. The pathologic lesions in what may be called experimental influenza in animals closely resemble those seen in the lungs of men.

3. There is some evidence in favor of the view that

---

(4) Brit. Med. Jour., March 22, 1919.

the passage of the virus from one animal to another may raise its virulence.

4. Inoculation of the filtered and unfiltered sputum taken from cases of influenza, especially at an early stage of the disease, has been found to produce lesions in the lungs in a high production of inoculated animals. The inoculation of blood may not always produce such striking results.

5. A minute microörganism of a coccoid shape may be grown by Noguchi's cultural methods from: (a) the kidney of infected animals; (b) the filtrates of lung tissue, and (c) the filtered sputum from cases of influenza. The cultures have been carried to the third generation by direct culture. The cultures when inoculated into animals produce typical experimental influenza lesions, and cultures can be recovered again from the animals so inoculated.

6. In view of these findings, the authors consider that there are very strong grounds for considering that: (a) the organism isolated by them is capable of passing through a filter; (b) that it is in all probability the cause of influenza as seen today.

**Pathologic Anatomy and Bacteriology of Influenza.** Pathologic anatomy and bacteriology of influenza, as seen in the epidemic of the autumn of 1918, is discussed at great length by B. Lucke, T. Wight and E. Kime.<sup>5</sup>

The studies on which this article is based were carried out at Camp Zachary Taylor and Camp Knox, Kentucky.

Necropsies, with routine bacteriologic cultures were performed throughout the entire epidemic, so that a fairly definite picture of its various stages could be formed. The investigation here reported was limited to 126 definitely proven fatal cases of influenza. These were selected from a considerably larger number by ruling out all patients who clinically gave evidence of preëxisting disease, such as tuberculosis or measles, or where such evidence was found at the necropsy. Thus the morbid changes encountered may be looked on as primarily representing the end-results of the virus of influenza and its commensals.

(5) Archiv. Int. Med., August, 1919.

This article occupies eighty-four pages and is concluded by an excellent summary of the various facts brought out in it. This summary is utilized entirely and presents a good review of the article.

In the first place it was found that influenza is greater among whites than among negroes, but the mortality rate is higher among the latter.

The average duration of life was fourteen days; in the early part of the epidemic the average duration of life was considerably shorter, and in the latter part considerably longer.

The anatomic and bacteriologic findings vary with the stage of the epidemic and of the disease, and depend to a certain extent on the endemic bacterial flora. Earlier in the epidemic the disease was more fulminating and during this time the *Bacillus influenzae* was most often found; as the epidemic progressed and the attacks lengthened, secondary invaders appeared more and more frequently and corresponding anatomic changes were found.

Influenza produces widespread changes throughout the body, and while the lungs commonly present the most spectacular lesions, pronounced alterations are also encountered in the nervous, cardiovascular and other systems.

The most general changes produced by influenza are pronounced congestion, hemorrhages, toxic degenerative lesions and hemorrhagic inflammations. Hyperemia and hemorrhages are especially striking in the meninges, brain, serous membranes (petechial hemorrhages), skin (intense cyanosis, purpura hemorrhagica), lungs, spleen, liver and kidneys. Example of toxic degenerations are Zenker's hyaline degeneration of the rectus muscles, conglutination and hyaline thrombosis, hyaline degeneration of vascular walls, hyaline degeneration of germinal centers of splenic follicles, focal necrosis of the liver, pancreas and suprarenals, toxic ganglionic changes and edema in the nervous system, and cloudy swelling of parenchymatous organs. Hemorrhagic inflammations are exemplified in early pneumonitis and pachymeningitis; productive inflammations are uncommon and confined to the later stages of the disease.

The true pneumonitis of influenza is characterized by extreme proliferation of pulmonary epithelium, pronounced hyperemia and hemorrhages. The commonly present secondary invaders produced a pneumonitis which grossly and microscopically consists of a number of separate, dissimilar pathologic processes. Macroscopically, a lobular pneumonia, with a tendency to become pseudolobar, and with a mixed, smooth and granular cut surface, is present. Microscopically, there are four distinct types of exudates, often within the same microscopic section, but distinctly independent. These are: catarrhal, fibrinocatarrhal, fibrinopurulent and purulent.

Throughout the disease there is a relative paucity of polymorphonuclear leukocytes and a proliferation of the lymphoid tissue; this would seem to point to myeloid intoxication and to lymphoid stimulation.

Chronic influenza is characterized by relative absence of vascular changes, connective tissue proliferation and diffuse suppuration.

The influenza bacillus, although not found in every case, was present in a sufficiently high percentage, and often enough in acute fatally ending infections to consider it, if not the prime cause, at least the most important indicator of epidemic influenza. At all events its appearance with the epidemic and its relative absence prior thereto, using the same cultural methods, strongly strengthens the assumption of its pathogenic rôle.

*Bacillus influenzae* was easily cultivated early in the epidemic and during the recrudescence of the last period, and this corresponded with the fulminating pathology of these stages.

As the patients lived longer and the epidemic progressed, bacterial agents, well-established at this post as the cause of respiratory tract disease, notably the non-hemolytic streptococcus and pneumococcus, appeared as secondary invaders and modified the bacterial readings and anatomic changes.

The non-hemolytic streptococcus, it should be stated, was a frequent commensal in the earliest part of the outbreak.



It is noteworthy that all the above secondary invaders were more fatal in symbiosis than alone.

Later in the epidemic, the hemolytic streptococcus assumed the ascendancy, as a tertiary invader crowding out the secondary invaders, and was of especial importance in cases of long duration. *Staphylococcus* and *M. catarrhalis* made their appearance toward the end of the epidemic and to some extent modified the pathology.

The authors enter a plea for the reading and recording of total flora and their symbiotic relationships; by this means too great weight would not be placed on single observations, like typing of pneumococci. Furthermore, in the study of this disease, observation should be made on the stage of the epidemic and the individual cases. By this method the proper relations of the various organisms can be calculated.

**Gross Pathology of Influenza.** A brief account of the gross pathologic changes seen in fifty-six necropsies on bodies that had died of epidemic influenza between Sept. 18 and Nov. 17, 1918, at the Walter Reed General Hospital, are recorded by M. W. Lyon,<sup>6</sup> jr.

In the patients the average duration of life from the date of onset was 12.4 days. The shortest illness was three days and the longest thirty-five days in a case of pneumococcus empyema.

The appearance of the body after death was in most instances characterized by a cyanotic condition of the neck, the ears and the adjacent portions of the face and shoulders. Equally conspicuous, was a brownish or reddish brownish fluid about the nostrils and the mouth. Most of the necropsies were done on individuals who appeared between 20 and 30 years of age. About five appeared to be between 30 and 40. The average number of leukocytes per cubic millimeter in this series of fatal cases was 5,537, with extremes of 2,675 and 11,900.

In describing changes in the lungs and accessory structures the term "hemorrhagic pneumonitis" is used to designate one of the characteristic lesions of the disease and seen in all the cases. It was marked by intense congestion of the lung tissue and an abundance of serous fluid loaded with red cells in the alveoli. It was present

(6) Jour. Amer. Med. Ass'n, March 29, 1919.

in all lobes and nearly always most conspicuous in the lower lobes and toward the mediastinal side. In no instance did the process involve completely any entire lobe.

In three instances the hemorrhagic pneumonitis was essentially confined to one side, the left. In two the process was more pronounced in the upper lobes than in the lower. In none was the right lung involved when the left was not.

As to pneumonic processes it was found that more or less distinct consolidation was usually present somewhere in the lungs, although in eleven instances, 20 per cent., no real pneumonic process was observable, the only lung lesions being the hemorrhagic pneumonitis. The average day of death in these eleven cases was 7.7 with extremes of 3 and 16 days. In thirty-five of the cases the consolidated portion was of small size and might be termed a lobular pneumonia. This condition was no more frequently found on one side than on the other. Most often it was found in all the lobes, but was most pronounced in the lower lobes. In sixteen cases the pneumonic process was extensive enough to be of a lobar type of consolidation. Lung abscess was not found during this work. In many instances, however, had the patient lived, abscesses in all probability would have formed. The lungs were usually much increased in weight owing to pneumonic and hemorrhagic process or both. The average weight of both lungs together, including a few millimeters of trachea, was 1,953 grams, with extremes of 775 and 3,290 grams. One of the more or less striking, essentially constant, gross lesions of influenza was what may be termed hemorrhagic pleuritis. By this is meant a bright or dull red spotting seen through the pleura in the surface of the lungs. It appeared to be an extravasation of blood beneath the pleura or else an extensive and local dilatation of the vessels of the surface of the lungs. The amount and location of pleural effusions as found in this work were as follows:

#### AMOUNT AND LOCATION OF EFFUSION

	No.	Per Cent.
No effusion on either side.....	9	16
Effusion present only on left side.....	23	41
Effusion present only on right side.....	16	29

	No.	Per Cent.
When effusion was present on both sides it had the same volume on both right and left sides.....	4	7
It was larger on the left side.....	24	43
It was larger on the right side.....	19	34

In only two of the fifty-six bodies examined was empyema found. From the pus in one of these pneumococci were isolated and from the other hemolytic streptococci.

A fibrinous or purulent pericarditis was not found in any instance. A moderate serous effusion was often present, although the fluids were clear. They were often dark as though somewhat blood-tinged. *Streptococcus hemolyticus* was isolated from one pericardial fluid and pneumococci from two others. No evident pathologic changes of the heart were encountered. In twenty-seven protocols the right heart is mentioned as being moderately or slightly dilated, particularly the auricle, which was usually well-filled with dark fluid blood. The average weight of the heart was 322 grams, with extremes of 210 and 460.

From these findings, the author states that as shown by the gross pathologic lesions in fifty-six fatal cases of epidemic influenza at the Walter Reed General Hospital, the disease is one attacking primarily the respiratory tract in which are uniformly noted a peculiar and intense congestion of the lungs, with hemorrhage into the lung substance, having mainly a lobar type of distribution, the involved portion on section dripping blood and resembling a newly formed clot of blood; acute congestion of trachea and bronchi without a purulent exudate, pleuritis, characterized by subpleural hemorrhagic spots, and frequently by exudation of moderate amount of blood tinged fluid.

Nearly as constantly present are congestion of the kidneys and of the brain, parenchymatous changes in the liver, and acute bronchial lymphadenitis, and a moderate dilatation of the right heart.

Secondarily, a variety of other lesions developed, such as lobar and lobular types of pneumonia. The lobar types of pneumonia are not typical of the primary form of that disease. A moderate serous pericarditis may

develop; very rarely a serofibrinous pericarditis may arise. A true empyema may ensue as the result of the usual exciting organisms, but is uncommon. The secondary changes in the lungs appear to be due to various organisms of greater or lesser virulence which happen to be in the respiratory tract at the time of the original attack.

**Suprarenal Involvement in Influenza.** This study on the clinical evidence of involvement of the suprarenal glands in influenza and influenzal pneumonia was carried out by D. M. Cowie and P. W. Beaven,<sup>7</sup> of Ann Arbor, Michigan.

Attention is called to the fact that suprarenal insufficiency has been demonstrated in many forms of acute infection. It is also pointed out that the reports from the departments of pathology where suprarenal glands have been studied indicate that frequently there is not an anatomic change to coincide with symptoms that indicate a clinical deficiency from these organs. The chief symptoms of suprarenal insufficiency are asthenia, prostration and lowered blood-pressure. In the patients suffering from influenzal pneumonia who were studied by these authors, the above findings were invariably present. But there were also other symptoms common to the disease which were characteristic of acute suprarenal insufficiency not of influenzal origin, such as nausea, vomiting, abdominal pain (epigastric and appendiceal), pains in the back and even tenderness on pressure over the back muscles and, in a few cases, diarrhea.

Tests used for determining the presence or absence of suprarenal insufficiency were first blood-pressure. In the cases in which blood-pressure was studied, five were complicated with pneumonia, and twenty were uncomplicated influenza. The average systolic pressure of the pneumonias was 99, and that of influenza was 115. These figures are considered as indicating a lowered pressure. The authors say that one can conceive of the demand for epinephrine by the toxin of an acute infectious disease being so great as to exhaust the suprarenals and other chromaffin tissues, and thus cut off one of the

(7) *Archiv. Int. Med.*, July 15, 1919.

potent factors in sustaining normal blood-pressure. They point out that in acute infectious diseases the toxins produced frequently call for the endocrine products to combine with them in a neutralization process. The criticism might be made that in acute infection the power of the heart muscle is so reduced as to produce a lowered blood-pressure and other symptoms that are named above as typical of suparenal deficiency.

In the patients studied in the present work, the authors were unable to demonstrate evidence of significant weakened heart action. To them it seems credible to regard the lowered blood-pressure in influenza and influenzal pneumonia as due to causes other than those of myocardial origin. They think that it may be considered as endocrinal.

The effect of prolonged administration of epinephrine was studied next. Of five influenza patients who were selected to test out this point, one was in the acute stage of the disease and was found later to be developing pneumonia at the time of the test. This patient's systolic pressure was 119 before the epinephrine was given. He was given 10 minims of epinephrine intramuscularly four times daily for three days. At the end of this time his pressure was found to be 131. The last measurement being made five hours after he had received his last injection of epinephrine. A study of the blood sugar in these patients was made next. Such determinations were made on the blood from thirteen patients who suffered from influenza, and on eight who had influenzal pneumonia. The blood sugar was found to be always within normal limits.

Next a study of blood changes following the intramuscular injection of 1 mg. of epinephrine was determined. It had been determined previously that the injection of 1 mg. of epinephrine causes a rise in blood sugar promptly, but this returns to normal within a period of two hours. It was found that following the injection of 1 mg. of epinephrine, influenza patients developed an increase in blood sugar and that this did not return to normal for a longer period than is found in a normal subject. In some instances it continued for a period of seven hours. The authors believe that these sustained



blood-sugar curves support the idea that endocrinal function is a factor in influenza and influenzal pneumonia and that the degree of endocrinal involvement is proportional to the prostration.

A further study of the blood-sugar curves after the ingestion of glucose was made: 1.75 grm. of glucose per kilogram of body weight was administered to the patient, and there was found a delayed return of blood sugar to normal; that is, the period was longer than three or four hours, as is observed in those patients who are known to have endocrinal involvement. Prolonged blood-sugar curves were found in five out of six patients who were given glucose at the rate mentioned above. These variations from normal are taken as lending further support to the idea that influenza affects the internal secretory system.

Concerning the therapeutic effect of epinephrine in influenza, the authors use the intramuscular method, giving from 10 to 15 mm. every four hours, four times daily. It was found that almost invariably the patient reacted with palpitation, complained of nervousness, slight headache, and increased lassitude, and occasionally marked twitching occurred. It was concluded that epinephrine, so administered at least, was of little if any benefit, and it was discontinued for these reasons. They state that possibly the proper method of administering epinephrine has not yet been found.

**Acquired Immunity to Influenza.** The observation of an acquired immunity to influenza as indicated by a recurrent epidemic in an institution, is recorded by J. H. Hamilton and A. H. Leonard.<sup>8</sup>

During the early part of November, 1918, there occurred an epidemic of influenza in the State Training School for Girls at Mitchellville, Iowa. At this time seventy-six of the girls had the disease. The second epidemic occurred in January, 1919. This second epidemic was practically limited to the cottages that had escaped the ravages of the November epidemic. The outstanding feature of the second visitation of the disease, was the fact that those who had recovered from influenza were immune to a second attack of the disease. This evidence

(8) Jour. Amer. Med. Ass'n, March 22, 1919.

tends to prove that immunity from influenza can be acquired from having an attack of the disease, and that the duration of this acquired immunity is at least two months.

The students of this institution were all between 12 and 18 years of age. The fact that 158 out of 180 of these young people developed the disease either during the first or the second epidemic, also suggests that there is a small percentage of approximately 12 per cent. who are naturally immune to influenza.

**Immunity Reactions to the Influenza Bacillus.** The object of this short communication by W. J. Wilson<sup>9</sup> is to show that Pfeiffer's bacillus causes a very pronounced immunizing response on the part of the influenza patients and that this indicates that its presence is no mere coincidence, but that it is in some important way associated with the diseases.

This investigation comprised the examination of forty-three separate specimens of blood. Ten of the specimens were from cases that were definitely not influenza, but included such conditions as vaccinia, mumps, bronchitis, etc. In all of these, no agglutinins for the *B. influenzae* were found. The remaining thirty-three cases were typical examples of influenza of a severe type and all the patients were suffering from or were convalescing from bronchopneumonia at the date of the examination. As this investigation was made toward the close of the epidemic in Belfast, the findings deal only with cases presenting lung complications, and the author is unable to say whether agglutinins are present where the lungs escape.

Of the thirty-three, the blood serums of eleven showed distinctly the presence of agglutinins for Pfeiffer's bacillus. It was found that the positive cases were all still running a temperature, while those that were negative had been afebrile for periods varying from six to thirty-two days. The study of three cases showed that the agglutinins very rapidly disappear from the blood when the patient becomes convalescent.

From this and from animal experiments with the organism, it is concluded that agglutinins for Pfeiffer's

---

(9) Lancet, Oct. 4, 1919.

bacillus early appear in the blood of cases of influenza. The titer may be as high as 1 in 1000.

These agglutinins rapidly diminish as soon as the temperature falls and are absent at the end of a week's convalescence. These agglutinins for the strains of bacilli studied by the author are absent from the blood of normal individuals and of influenza convalescents, even when tested for a dilution of 1 in 2.

Complement can be fixed by an immune body present in the serum of influenza patients at the height of or early in the disease.

The intravenous injections of rabbits with cultures of Pfeiffer's bacillus causes death in a few hours and the congestion and edema found in the lungs may account for the dyspnea and asthenia which precede the fatal issue.

**Clinical Observations on Epidemic Influenza.** Epidemic influenza, as seen in the Johns Hopkins Hospital, is reported by A. Bloomfield and G. A. Harrop,<sup>1</sup> jr.

The main statistical facts of the epidemic are summarized in the following table and chart, which are based on the study of 268 patients admitted between Sept. 24 and Oct. 20, 1918:

GENERAL STATISTICS OF THE INFLUENZA CASES IN  
THE JOHNS HOPKINS HOSPITAL

	No.	Per Cent.
Total cases .....	268	....
Total deaths .....	13	4.8
Total number developing pneumonia .....	41	15.3
Total deaths among pneumonia patients.....	13	32.0
Total deaths among patients in hospital from start of disease .....	7	2.7
Total number of patients in hospital from start of disease developing pneumonia .....	28	11.0
Total number of patients admitted with frank pneu- monia .....	13	....
Total deaths among patents admitted with pneu- monia .....	6	46.0
Total deaths among patients developing pneumonia in the hospital .....	7	25.0
Total number of nurses admitted.....	123	....
Total number developing pneumonia.....	12	9.8
Total deaths .....	3	2.4
Total deaths of patients developing pneumonia.....	3	25.0

(1) Bull. Johns Hopkins Hosp., January, 1919.

Practically all of the cases recorded here were seen from the very start, and it was possible to study in detail the earliest symptom and the mode of onset. From these observations, it was clearly apparent that the disease is not primarily a local respiratory infection, and that it presents a clean-cut definite clinical picture quite independent of pulmonary complications. It is also emphasized that influenza as seen now corresponds in detail with the descriptions of the previous pandemics. It is undoubtedly the same disease.

The disease as seen by Bloomfield and Harrop was ushered in by two groups of symptoms. In the first place the constitutional reactions of acute febrile disease—headache, general aching, chills, fever, malaise, prostration, anorexia, nausea or vomiting; and in the second place, symptoms referable to an intense congestion of the mucous membranes of the nose, pharynx, larynx, trachea, the upper respiratory tract in general, and of the conjunctivae. Superficially, the onset seems to vary in different cases, depending on whether one or other of these sets of symptoms predominates, but a striking essential similarity prevails, which is most obvious during the height of the epidemic, when the disease runs more constantly true to type. For this reason it seems misleading to divide the ordinary run of cases into respiratory, abdominal and nervous. It would seem better to reserve the last term for those patients showing organic lesions of the nervous system or psychoses more outspoken than the usual temporary depressions.

Three distinct types of invasion were noted—abrupt invasion, gradual invasion and invasion with intermittent symptoms.

Concerning the physical findings, the authors state that although evidence of gross lesions is absent in uncomplicated cases, the physical findings are none the less clean cut and typical.

Early in the course of the epidemic there was noticed an unusual bright red appearance of the throat in most of the patients, and more careful study of subsequent cases showed this to have striking and constant features. The changes in the mouth usually become full-blown

during the first twenty-four hours of the disease. The most striking feature is a bright vermilion or scarlet injection of the pharynx, tonsils, pillars and soft palate. In many cases, this erythema extends over the entire mouth, and can be exquisitely demonstrated by pressure on the mucosa of the cheek with a spatula. In the most marked cases, the entire oral cavity has a flaming appearance.

The general appearance is most striking. In well-marked cases, there is an intense, dusky, reddish-plum-colored erythema of the face, lips and upper chest, which usually fades off abruptly at the level of the breast, but may extend over the entire chest and back, and occasionally involve the arms and legs. The entire facies has a remarkable suffused look, not unlike that seen in polycythemia vera. It is, however, quite different from true cyanosis, and studies of the oxygen-combining capacity and content of the blood in these patients gave normal results.

Bacteriologic studies of these patients were made by Dr. Howard, and they fail to bring evidence that the bacillus of Pfeiffer is the cause of epidemic influenza.

Blood cultures made at onset in the acute cases were uniformly negative and it was only in the terminal stage of the complicating pneumonia that organisms appeared in the blood. Pneumococci or streptococci were isolated in a few instances but no influenza bacilli. Nasopharyngeal swabs made at onset showed the usual mouth flora. Gram-negative bacilli were seen in smears in some of the cases, but only once as the predominating organism. In three instances of post-influenzal pneumonia, the Pfeiffer bacillus predominated in the sputum culture but in most cases the pneumococcus, green streptococcus and other organisms were mainly present.

The conclusions presented from the observations made by these authors are that: Epidemic influenza in 1918 was clinically identical with the disease as seen in previous pandemics. It is not primarily a local disease of the respiratory tract. It presents a definite and characteristic clinical picture quite apart from the pulmonary complications. The main features of the uncomplicated disease are a constant set of symptoms.



characteristic erythema and appearance of the mouth, fever of determinate duration and leukopenia. Proof is lacking that the Pfeiffer bacillus is the primary cause of uncomplicated influenza.

**Report of Epidemic at Camp McArthur.** An extensive detailed report of the influenza epidemic as seen at Camp McArthur, is reported by L. S. Medalia,<sup>2</sup> Major, U. S. Army.

The investigation dealt with etiology, bacteriology, pathology and specific therapy. Concerning the specific therapy, the author says that the first few cases that came to necropsy, showed bacteriologically that a predominating Type IV pneumococcus infection associated with the influenza was being dealt with.

It was therefore decided to make use of the polyvalent into pneumococcus serum as a routine treatment in these pneumonias. The comparative mortality incidence in the influenza pneumonia cases before and after serum treatment was begun are tabulated. From these it would seem that there is but a slight difference between the two. However, by leaving out from the serum-treated cases those patients who received serum while in a moribund condition, as a last resort, the difference in the mortality is quite marked: 7.6 per cent. against 34 per cent. in favor of the serum-treated cases. It is the author's opinion that the polyvalent serum was of value in the influenzal pneumonia cases in this camp.

From the extensive data tabulated in this paper and the discussion of methods used, the following excellent summary is presented:

The influenza bacillus was found in the epidemic in this camp to be the predominating organism. Out of 2279 sputums examined, 76.8 per cent. were found positive to this organism. The pneumococcus was the most important associated organism being found in 53 per cent. of the total sputums examined. The examination of contacts for influenza carriers as a means of prevention, though possible, was found impracticable. The spread of this disease is too rapid, and can not be prevented by the examination of contacts and the isolation of carriers, unless perhaps in very small bodies of troops.

(2) Boston Med. and Surg. Jour., March 20, 1919.

The type determination on 400 cases of influenza-pneumonia conformed to the following: Type I, 0.23 per cent.; Type IIa, 3.4 per cent.; Type II, 1.8 per cent.; Type III, 1.1 per cent.; and Type IV, 85.8 per cent.; undetermined, being bile insoluble, 8.6 per cent. The *B. influenzae* was found in 54 per cent. of the bronchopneumonia sputums that were typed. Blood cultures made on 233 cases showed thirty-four, or 14.6 per cent. positive. Of the thirty-four cases, thirty-one or 94 per cent. were found to be pneumococcus. *B. influenzae* was found in two cases or 5.8 per cent. (one mixed with pneumococcus). The high percentage of positive *B. influenzae* found in the bronchopneumonia cases that came to necropsy, in the lungs, pleural cavities, the heart, the spleen, culturally, and in the stained tissue of the lungs and spleen, is further evidence of the causative relation of *B. influenzae* to the bronchopneumonia. It also demonstrates the frequency of the organism in the circulation. The sixty-one consecutive necropsies showed 92 per cent. to be bronchopneumonia: 8 per cent. lobar.

Empyema (bloody-sero-fibrino-purulent) was a constant finding, being present in over 75 per cent. of the cases.

**Serum Reactions in Influenza.** There is apparently little information on the serology of influenza which is of certain etiologic or diagnostic importance. After a brief reference to this scanty literature, F. P. Gay and D. H. Harris,<sup>3</sup> who worked at the Yale Army Laboratory School in New Haven, present experiments dealing with the subject. Several rabbits were immunized by from six to eight injections, the majority intravenously, but a few subcutaneously, of a mixed vaccine comprised of equal parts of ten different strains of *B. influenzae*. These strains were uniformly grown on a "chocolate" medium, prepared by adding 5 per cent. of defibrinated rabbit or human blood to 5 per cent. glycerol agar at a temperature of 95° C.

The rabbits received injections beginning with 0.5 c.c. of a thick suspension of the mixed cultures, killed by the addition of 0.5 phenol at first. On subsequent

(3) Jour. Infect. Dis., November, 1919.

injections, living cultures were employed. It was found that injections could be given at short intervals without producing any symptoms in the rabbits except slight loss in weight. The serum of these animals was tested after six or eight injections. It was found that the serum of rabbits immunized in this way gave for the most part negative immunity reaction. Fixation bodies were found in high dilution, using a preparation of the same mixed cultures as antigen. Agglutination reactions were negative when incubated for a short period of 37° C., but positive in from three to six hours at 55° C. The immune serum failed to react with two strains of *B. influenzae* that had not been used in immunizing, thus suggesting the existence of separate groups of *B. influenzae*.

The serum of acute influenza cases gave a positive agglutination reaction at 55° C. in dilutions of 1:80 and above, in the majority of instances (88 per cent.) with one of the strains of *B. influenzae* tested. A few tests with another recently isolated strain from this epidemic were also positive in a few instances. Another strain was uniformly negative. Fixation reactions were negative in all but one case with a mixed antigen.

The serum from individuals who had recovered from influenza gave agglutination reactions at 55° C. in about two-thirds of the instances. Fixation reactions were negative.

The serum of individuals who had been vaccinated gave agglutinations at 55° C. in 45 per cent. of the cases. Fixation reactions were positive in 40 per cent.

The normal cases, although few in number, were uniformly negative.

**Prophylactic Use of Mixed Vaccine Against Influenza.** Mixed vaccines were used as a prophylactic against pandemic influenza and its complications, at the Naval Training Station, San Francisco, by A. J. Minaker and R. S. Irvine.<sup>4</sup>

In the light of observations that had been made by various workers over the country, before the epidemic reached San Francisco, the authors used a vaccine for

---

(4) Jour. Amer. Med. Ass'n, March 22, 1919.

each cubic centimeter of which there were the organisms indicated in the accompanying table:

#### COMPOSITION OF MIXED VACCINE

	No. of Bacteria
<i>B. influenzae</i> , Rockefeller strain.....	5 billion
<i>Pneumococcus</i> Type I, various strains.....	3 billion
<i>Pneumococcus</i> Type, II, regular and irregular, various strains .....	3 billion
<i>Pneumococcus</i> Type III, one strain.....	1 billion
<i>Streptococcus hemolyticus</i> , two strains.....	100 million

The vaccine was administered subcutaneously at about the insertion of the deltoid muscle in doses of 0.8 and 0.5, and 1 c.c. at three day intervals. In all 11,179 persons were inoculated, composed of four distinct groups.

Tabulated results are given to show the difference of incidence and mortality among the inoculated and uninoculated. From the facts obtained by the authors, they conclude that undoubtedly a noteworthy degree of protection against influenza and its complications was obtained by means of a mixed vaccine freshly prepared from the predominating etiologic bacteria. These observations should also encourage further work along the line of immunity against pneumonia.

• They state further that to this end an attempt is now being made to regroup the Type IV pneumococcus with the object of adding it to a vaccine when needed.

**Prophylactic Inoculations in Influenza and Pneumonia.** This fourth paper on studies on influenza and pneumonia by E. C. Rosenow and B. F. Sturdivant,<sup>5</sup> of Rochester, Minn., deals with further results of prophylactic inoculations. The first stages in this part of the work consisted of the preparation of large amounts of vaccine and sending it free on request to numerous physicians, on condition that reports of the results be returned.

In the present paper, essential points in the preparation of the vaccine are emphasized, and further results of the use of this vaccine are reported and a record of certain immunologic experiments is presented.

The formula of the vaccine used is as follows:

(5) Jour. Amer. Med. Ass'n, Aug. 9, 1919.

## FORMULA OF VACCINE

Pneumococci, Types I (10 per cent.) and III (6 per cent.) .....	30 per cent.
Pneumococcus Group IV and the allied green-producing diplostreptococci described .....	40 per cent.
Hemolytic streptococci .....	20 per cent.
Staphylococcus aureus .....	10 per cent.

The vaccine reports were returned from 530 physicians and were sufficiently complete for compiling the results indicated and shown in the following table:

## RESULTS AS REPORTED IN QUESTIONNAIRES FROM ALL SOURCES

Disease: Incidence for 1,000 Persons					
Groups	Total Number	Acute			
		Influenza	Edema of Lungs	Pneumonia	Empyema
Vaccinated once.....	26,936	118.2	3.1	8.7	0.29
Vaccinated twice ....	23,348	97.0	0.77	3.04	0.17
Vaccinated 3 times...	93,476	87.9	0.8	4.4	0.18
Not vaccinated .....	345,133	281.8	4.4	21.0	0.83

Deaths: Incidence for 1,000 Persons							
Groups	Acute Edema Pneumonia Empyema Meningitis Encephalitis Total						
	of Lungs	monia	ema	gitis	litis	Deaths	
Vaccinated once ....	0.14	2.6	0.07	0.18	....	3.0	
Vaccinated twice ...	0.47	1.9	0.04	0.21	....	2.62	
Vaccinated 3 times..	0.18	1.2	0.00	0.05	....	1.43	
Not vaccinated .....	1.7	2.37	0.07	0.15	0.03	8.55	

The total number of unvaccinated persons recorded in this table, represents the sum of the estimated clientèles of the various physicians reporting the cases, and averages about 1,200 for each. It is noted that the incidence of influenza, of acute edema of the lungs, of pneumonia following influenza and the number of deaths from all causes among the vaccinated are consistently lower than that among the unvaccinated. Moreover, the incidence of disease and deaths is lowest in the group of 93,476 persons who were vaccinated three times. The reports included in this table were from many states, but the largest number came from Iowa, Minnesota, and Wisconsin: 13,650 persons inoculated and 2,083 who died were grouped according to age by decades. The curves indicating the percentage in each run roughly parallel.



The chief points of interest in regard to this work are brought out in the summary, which is reproduced here entirely.

"The immunologic and animal experiments reported elsewhere indicate that the mixed vaccine used by us contained the important bacteria as they occur in influenza and the accompanying pneumonia, and that a relatively large number of strains of the green-producing streptococci which appear to have a specific relationship to the initial attack were included. The reports included results obtained under the most varied conditions, from many communities covering a wide range of territory. In some communities the mortality rate was excessively high, in others comparatively low. The number of persons inoculated is sufficiently large to make the statistical figures fairly accurate. The period of observations was from three to seven months. The incidence of influenza and pneumonia as reported to us is probably far from exact, but the percentage of error should be about the same in the vaccinated and unvaccinated groups. Indeed, if a difference exists, the number of cases reported among the vaccinated might be expected to be proportionately higher because, even though no protection was promised, the fact that influenza occurred after the vaccinations were taken would naturally lead to a higher percentage of reports to the physician who gave the inoculations. The average incidence of influenza and pneumonia in the group inoculated three times is about one-third that of the uninoculated group.

"The average mortality rate in the uninoculated, as reported, approximates the mortality rate (5.4 per cent.) of sixteen large cities of the United States as given in *Public Health Reports* for February 7. The average mortality rate in the group inoculated three times is about one-fifth that of the uninoculated. A definite although a smaller degree of protection appeared to be afforded to those who took only one or two inoculations. From a study of a series of hospital cases of influenza, it is found that the tendency to the development of pneumonia in the vaccinated is about one-third as great as among the unvaccinated and that the mortality in the former is about one-fifth as great as in the latter.

The number of completed vaccinations in pregnant women is not large enough to give exact figures, but the results indicate clearly that a definite degree of protection was afforded in this group of individuals.

"It appears from all the facts at hand that by the use of a properly prepared vaccine it is possible to rob influenza of some of its terrors.

"The preliminary results from the use of more than 500 doses of this vaccine suspended in oil, the immunologic studies and the results from the use of pneumococcus lipovaccine reported by Femmel and by Cecil and Vaughan suggest strongly that both the degree of protection and the duration of the immunity may be materially increased by the use of lipovaccine over that reported in this paper from the use of the saline vaccine."

**Prophylactic Vaccination Against Influenza.** This phase of the influenza problem is discussed by G. W. McCoy,<sup>6</sup> Director of the Hygienic Laboratory, U. S. Public Health Service at Washington.

In considering opinions as to etiology of influenza and influenzal pneumonia, the discussion brings out the opinion that the cause of influenza remains in doubt at present.

When the etiology and pathology of influenzal pneumonia are considered, there is found a rather general opinion that pneumonia is due to Pfeiffer's bacillus, or to the secondary invasion by organisms of acknowledged pathogenicity, particularly the various types of pneumococci, the streptococci, especially those known as hemolytic and, less commonly, Friedlander's pneumobacillus or the staphylococcus.

Concerning the experience of various workers with prophylactic vaccination, those who have used a vaccine made from influenza bacillus as a prophylactic are first considered.

McCoy states that when the influenza vaccine was submitted to such critical tests as the inoculation of approximately half of the individuals in institutions, or in other large groups, its failure became apparent. A few examples of this are worth citing, and the following table presents results obtained by Hinton and Kane, who were

(6) Jour. Amer. Med. Ass'n, Aug. 9, 1919.

able to vaccinate about half of the patients at an epileptic colony, long enough before the disease became prevalent in the institution to justify the drawing of conclusions from their data.

#### EFFECT OF INFLUENZA BACILLUS VACCINE AS A PROPHYLACTIC

	Vaccinated		Not Vaccinated (controls)	
	No.	Per cent.	No.	Per cent.
Number of persons .....	461	....	518	....
Cases of influenza.....	163	35.4	178	34.3
Deaths .....	28	17.6	24	11.5

On the basis of this experiment, Hinton and Kane reached the obvious conclusion that the vaccine was without value.

Vaccine from streptococcus and other organisms are not considered. It is found that no results have been published that establish streptococcus vaccine as being of any value when used for purposes of prophylaxis.

The polyvalent vaccine prepared by Rosenow was made from various types of pneumococci, pneumococci of Group IV, hemolytic streptococci, *Staphylococcus aureus*, and the influenza bacillus, all of which had been recently isolated.

Dr. Rosenow is said to have felt that this vaccine should be prepared for use in any community from the strains of organisms there prevailing, and that a vaccine adjusted to meet the needs of one locality might not meet those of another. These figures were given for protection and are encouraging but do not lend themselves to critical analysis. The discussion here of results reported by those who administered the vaccine prepared by Rosenow, or vaccines prepared according to his specifications, is to the effect that whenever used and properly controlled its results were as the others, that is, without evident value as a protection against the disease.

In conclusion, McCoy states that the general impression gained from uncontrolled use of vaccines is that they are of value in the prevention of influenza, but in every case in which vaccine has been tried under perfectly controlled conditions, they have failed to influence

in a definite manner either the morbidity or the mortality.

**The use of Vaccines as a Prophylactic Against Influenza in British Troops.** This report deals chiefly with measures against influenza as carried out by J. W. Eyre and E. C. Lowe.<sup>7</sup>

The tabulated results observed among New Zealand troops in the United Kingdom, during the epidemic of 1918, are presented in the following table:

	Inoculated	Uninoculated
Average total strength N. Z. troops in U. K., 21,759.....	Approx. 16,104	Approx. 5,700
Incidence of influenza (3,366 cases).....	1.3%	4.1%
Mortality in all cases.....	9.28%	2.2%
Mortality in severe and complicated cases .....	8.0%	23.0%

The vaccine used to inoculate these troops was called M. C. V. or mixed catarrhal vaccine. The organisms contained in it and the size of the first and second doses are indicated in the following statement:

Organism	First dose Millions	Second dose Millions	Organism	First dose Millions	Second dose Millions
Pneumococcus .....	50	100	M. catarrhalis .....	25	75
Streptococcus .....	10	50	B. pneumonia .....	50	100
B. influenzae .....	10	30	B. septus .....	50	100
Staph. aureus.....	200	500			

**Vaccine Therapy in Treatment of Influenzal Bronchopneumonia.** This paper dealing with the treatment of influenzal bronchopneumonia with special reference to vaccine therapy is one of a number of papers in a symposium on this subject of influenza.

In this discussion, W. H. Wynn<sup>8</sup> states that if expectant treatment were always successful, specific treatment would not be required. But faced with the tragic loss of healthy young men and women with whom expectant treatment should have had its best chance, the question of an attempt at giving direct aid immediately arises. The only specific treatment available is with vaccines, and it is hoped that encouraging results can be proven, as resulting from their use.

(7) Lancet, April 6, 1919.

(8) Practitioner, February, 1919.

Before all things, the author places absolute rest and free ventilation in the treatment of bronchopneumonia. He also discusses diet, and says that the useful routine diet is milk, citrated if there is vomiting, and albumin water, 5 oz. of each alternately every two hours. Patients are usually thirsty and will take an abundance of plain water or lemon water, but unless insisted upon, the need of water is usually overlooked. Many persons still think that it is dangerous to drink plain water, and this notion must be overcome.

The records of twelve patients who suffered from pneumonia and who were treated with vaccine, are presented in considerable detail. Wynn says that the striking feature in the use of vaccine has been the almost constant fall in temperature, following the injection. The earlier the injection is made, the more likely is the fall to be final. In patients injected after the second day, more than one injection is usually required before the temperature finally settles. Occasionally the first dose fails to cause a drop in the temperature and a second larger dose is required to bring this about. If the fall of temperature occurred alone, or if it were followed by collapse or other bad signs, it would not be desirable, but the fall is associated with improvement in the aspect, and in the pulse and respiration rate, which indicates that it is due to a definite immunizing response.

The vaccines that were used by Wynn on these patients contained several strains of pneumococci, streptococci and *B. influenzae*. In a few instances *B. friedlander* was added, because the sputum in these patients contained this organism. In some localities it might be desirable to add *M. catarrhalis*.

Until the bacteriology of the disease has been more thoroughly worked out, vaccine treatment must necessarily be largely empirical, but experience has shown, he says, that these three organisms are most commonly associated with influenzal bronchopneumonia, and a vaccine composed of them gives good results. The information so far collected points to influenza bacillus being the cause of cyclical epidemics, and having the power of enhancing the virulence of the organisms with which it is associated. It is the Bolshevik agent stirring up strife



in many lands among a bacterial population of itself inclined to local outbreaks of virulence. These organisms have been used in varying doses. The present plan of the author is to give them in equal numbers, as the cases cited show the doses have varied in size.

For an adult man it is now recommended that a dose of from 80 to 100 millions of each organism be given. For an adult woman 60 to 80 millions, for a child of 10 to 12 years from 30 to 50 millions, for a child of from 2 to 3, from 10 to 20 millions.

Symtomatic treatment of this type of pneumonia is discussed briefly. With the digitalis and strophanthus group it is said that one reaches a highly debatable ground. Their use has again risen in favor, but there is no experimental evidence to support the giving of digitalis to the heart in fever.

Following this opinion is one quite as radical, which takes the view that alcohol is of practically no value in the treatment of this condition.

Of other drugs, he says: Caffeine citrate, 5 grs. three times a day in a strong cup of coffee, frequently acts well. In collapse, saline infusions with glucose 5 per cent. injected subcutaneously or very slowly into a vein have a distinct life-saving value and are too seldom used.

Finally, he says that the confirmed therapeutic optimist can face with equanimity these cases of failure from toxic exhaustion. It is difficult to refrain from giving some drug; but the truth must be faced that there are no drugs of undoubted value, no drugs, even of which the indications for administration are clear. Our real hope lies in the establishment of sound lines of specific treatment, so that by its early administration bronchopneumonia may be robbed of half its terrors.

**Bacterial Protein Injections in Influenza.** A brief description of methods used and results obtained by bacterial protein injections in influenzal pneumonia is recorded by D. Roberts and E. G. Cary.<sup>9</sup>

[This title is misleading. The method is nothing more than a polyvalent vaccine, consisting of heat killed bacteria suspended in normal salt solution. The method is

(9) Jour. Amer. Med. Ass'n, March 29, 1919.

the one most commonly used in the administration of dead bacterial vaccines.—B.]

They used a saline suspension of heat-killed organisms so that each cubic centimeter contained 100 millions influenza bacilli, 100 million pneumococci, Types I, II and III, 100 million streptococci and 100 million staphylococci. From the standpoint of establishing an immunity, that was hardly hoped for, because the vaccine was not sufficiently polyvalent. At first, 0.5 c.c. of the suspension was used as the initial dose, and doubled daily until four doses had been given. Later, 1 c.c. was used as an initial dose, succeeding ones being regulated by the amount of reaction obtained.

Two hundred patients were treated in this way and studied, and from this experience the authors state that there are no untoward results whatsoever. The severely ill are never made worse. It was also found that the results were unsatisfactory if a reaction did not follow the injection, and the results were usually satisfactory if there was a sharp reaction. These rules are not without exception, however.

The relative mortality of patients treated in this way and those treated expectantly is shown by the fact that out of a total of eighty-six patients who were given expectant treatment, twenty-seven died, a mortality of 31.2 per cent. Out of a total of 200 patients who were given protein injections there were nineteen deaths, a mortality of 9.5 per cent.

The question arises at once as to whether the lowered mortality in the second group was due to the fact that it was later in the epidemic. It is not considered by the authors that there was a difference in the virulence of the disease in the two different groups of patients, although later in the season, after the second group had been treated, during the months of November and December, the virulence did seem to be somewhat lessened. They state that there can be no question that convalescence as judged by the return of temperature to normal came earlier in the protein injection group than in the other. Finally, in studying and recommending any new therapeutic procedure the greatest caution should be observed. The authors have endeavored to analyze critically the

results and see to what other factors the shortening of the disease and the lessened mortality in these groups of patients are due. They were forced to conclude that in the malady under consideration protein injections had a very definite therapeutic value and they are inclined to believe that the procedure will come to be accepted as useful in a wide variety of infectious diseases.

**Non-Specific Proteins in Treatment of Influenzal Pneumonia.** Results obtained by the use of this method of treatment of patients with influenzal pneumonia are recorded by Theodore Louis Squier,<sup>10</sup> of the Department of Internal Medicine, University of Michigan.

In spite of the fact that many articles have already appeared concerning the excellent results following non-specific protein therapy in influenzal pneumonia, the author feels that its value can not be over-emphasized. To attempt a detailed discussion of the merits of such treatment would be too much in this place, but the results obtained by treating four cases, the first two of which were treated with the idea in mind of combating the infection and supplying additional specific immune bodies as such, are recorded. The apparent failure of this method of treatment led to the more successful use of non-specific proteins in three cases. The records of these four patients are given in detail. A summary of the results is given, in which Squier states that a citrated blood transfusion which produced a severe reaction was followed by a drop in temperature, by crisis and by prompt recovery.

Two transfusions with immune blood which caused no reaction were followed by no change in the temperature, pulse, respiration or general physical condition.

When typhoid substance was used and a typical protein reaction obtained there was in each instance a sharp fall in temperature and a dramatic improvement in the patient.

These results have led Squier and his associates to believe that non-specific protein therapy has a very definite

---

(10) Jour. Mich. State Med. Soc., June, 1919.

and important place in the treatment of influenzal pneumonia.

[The reader's attention is directed to page 26 of this volume for remarks upon the intravenous injection of non-specific protein as a therapeutic agent.—B.]

**The Cardiac Complications of Influenza.** This subject is discussed by Sir James Mackenzie,<sup>1</sup> as a part of a symposium on the subject of influenza. He says that the cardinal vascular phenomena in serious cases of influenza are the same as in other cases of severe infection. The heart in all fevers reacts to three different stimulations: (1) the rise of temperature; (2) the toxins produced by the microbe; (3) the direct invasion of the heart by the microbe. All these may be present in the same individual in varying degrees. When life is endangered, the phenomena are very characteristic. The chief sign in all cases of danger is the early appearance of that dusky hue which every experienced clinician recognizes. The pallid cheeks with a slight tinge of blue, and the dusky red lips, are always signs of gravity in any form of infection. Coupled with this, there will invariably be an undue rapidity of the pulse—120—130—140—a minute with, it may be, a moderate temperature. The pulse often at first is full, but the beats are not strong nor is their force sustained; later the pulse becomes small and thready—a very ominous sign. The heart itself is increased in size, not usually to any considerable extent, and the sounds become soft and muffled, sometimes with systolic murmurs. These are the phenomena which indicate danger in all cases of pneumonia, bronchopneumonia, and bronchitis. When an attack of influenza threatens life, it is associated with the physical signs of these diseases and usually with delirium and unconsciousness.

The picture is really not one of heart disease, or lung disease or brain disease, but that of intense intoxication of these different systems. When the patient dies, it is not so much because of the heart failure, but from the intoxication, though no doubt evidence of damage can be found in the heart.

In the treatment of these severe cases, it is the man-

(1) Practitioner, January, 1919.

agement of the patient as a whole that helps, and here intelligent nursing is of most avail. Cleansing of the mouth and teeth, careful regulation of the bowels, sponging of the body and making it comfortable, discreet dieting, especially the avoidance of too much sloppy food, with small portions of solid foods that compel chewing, if the patient is conscious.

The author has not seen any patient with influenza in which damage was limited to the heart alone, such as occurs in rheumatic fever. That pericarditis, endocarditis and myocarditis occur along with lung complications has been repeatedly demonstrated postmortem, but the author has never seen a patient recover with damaged valves.

A number of patients who suffered with chronic heart disease before they developed influenza were observed. It was found that influenza did not in any way injure these patients. Every one, even those with advanced heart failure, passed through the attack safely.

When the after-effects of influenza on the heart are considered, it is found that the great majority of patients not only pass through the febrile stage of influenza with no sign of damage to the heart, but their recovery is rapid and complete. There are a number, even among those who seem to have had but a mild attack, and in whom convalescence is slow and protracted, and these may seem far from well for months or years after the attack. These cases are not cardiac in the sense that the weakness is due to some affection in the heart. It seems that the condition is rather one of poisoning which affects the body generally, but in which the cardiac manifestations are most in evidence. If, however, a careful study is made of the patients, other signs will be discovered.

Taking into consideration all the facts, it will be found that the weakness after influenza is not, properly speaking, entirely cardiac in origin. It is the outcome of injury to other systems, as well as to the heart, such as the central nervous system. Even when one finds such marked abnormalities as increased rate, systolic murmurs and an increase in the size of the heart, or the occurrence of irregular action due to extrasystoles, the cause of the



signs ought not be looked on as heart disease, but merely as part of the manifestations of general illness.

**The Heart in Influenza.** H. Eichhorst<sup>2</sup> finds that anatomic lesions are exceptional: In 2,411 grave cases, he found only six of mitral insufficiency (two proved by necroscopy), and two of serofibrinous pericarditis. He never encountered myocardial lesions, even microscopic. However, functional disturbances, and involvement of the cardiac sensory nerves are very common, even constituting one of the characteristic signs of the infection. Four principal clinical types can be made out:

1. Tachycardia is the rarest. The increased rhythm, occasionally very considerable, may appear during the febrile period, when it appears and disappears suddenly, despite the persistent fever; or it may come on during defervescence, and may be either transient or lasting. As a rule it is not noticed by the patient. On some occasions it may precede the usual manifestations of grippe by many days. In one of Eichhorst's patients it persisted as an initial and isolated symptom for 5 days.

2. Generally bradycardia is observed. This may ensue either during the height of the disease, pulse of 48 with fever of 104° F., the discordance being either temporary or permanent; or it may occur at the beginning of convalescence. Marked bradycardia may also be seen in the non-febrile cases. Rarely, it is accompanied by subjective sensations such as precordial oppression. Contrary to the tachycardia it tends to keep up for a very long time.

3. In the extrasystolic heart, the numerous extrasystoles may appear at the same stages of development as the bradycardia, as a rule very persistent, they may or not be accompanied with the well-known subjective sensations.

4. In the neuralgic heart which is very uncommon, and was noticed by Eichhorst only in young and vigorous men at the time of convalescence, the symptoms consist particularly of a sensation of stoppage of the organ, and of precordial pains radiating to the left shoulder, coming on in crises, recurring up to twenty times in a day.

The prognosis of all these troubles seems not very

(2) Cor.-Bl. f. Schweiz. Aerzte, Feb. 22, 1919.

serious, though they often oppose stubborn resistance to therapeutic measures. These consist of employment of valerian, quinine and strychnine, associated with abstention from fatigue and cardiac excitants.

**Intra-abdominal Complications of Influenza.** Intra-abdominal catastrophies associated with influenza are discussed by Smith.<sup>3</sup>

During the epidemic of influenza in 1918, which passed through the hospital in which the author was employed in three successive waves from June to December, several important abdominal complications were observed.

They are divided into three classes, comprising those directly due to a specific bacillus, those due to associated toxemia, and those which are coincident and noted as a warning to the surgeon. The first class includes infections of the general peritoneal cavity by organisms associated with the influenza epidemic. The infecting agent has always been the streptococcus and, so far as can be stated, it is a blood-borne or embolic lesion and takes the form of an acute streptococcus general peritonitis. An instance of this kind is cited in which the patient died.

The second class of intra-abdominal complications is that in which there is an acute toxic dilatation of the stomach produced by influenza. The record of one patient who developed this condition, and finally came to autopsy is presented.

A second patient who developed this condition was operated upon and the greatly dilated stomach was massaged and emptied of its gas three or four times. Hot saline was applied and pituitrin injected into the arm. The abdomen was closed and the patient returned to the ward. Pituitrin and atropine were continued and the feedings by mouth carefully restricted. After five days of typical influenzal chart and symptoms the patient recovered, no signs being apparent on examination of the chest.

In the third class of complications, the author places coincident acute abdominal lesions occurring during the influenzal attack and during convalescence. An instance of acute appendicitis that went on to a gangrenous state and ruptured is cited. The appendix was removed and

(3) Lancet, March 15, 1919.

the region drained. Soon after the operation the patient developed lobar pneumonia but recovered in spite of this.

Among general statements made in the way of conclusions, it is stated that during the epidemic of influenza, the chest should become more the province of the surgeon than is usual and should be minutely searched for any physical signs when a suspected abdominal lesion arises. The division of these conditions into three classes as outlined by the author may save a laparotomy in a patient who is already not in good condition. The infection of the peritoneum at such times is blood-borne and is not due to direct extension through the diaphragmatic lymphatics.

*Streptococcus endocarditis* is the jumping-off ground for peritoneal infections, but is not necessarily always present. Surgical interference with these cases of peritonitis has been of no avail, but this is not surprising when one studies the mortality during such an epidemic in which as yet intra-abdominal lesions have not been recorded.

Discretion in dietary is very necessary in the toxemic type as an overloaded stomach may become a danger. Persistent vomiting in cases of influenza toxemia should be regarded with suspicion. Although the evidence is as yet small, the condition of acute dilatation is proved, hence, early stomach washing and the use of pituitrin may save a patient where a *laissez faire* attitude will certainly end in death.

Therefore, the incidence of true abdominal catastrophes in a patient with influenza must always be kept in mind and suitable measures promptly undertaken.

**Influenza and Tuberculosis.** For reasons inadequately explained, it has been handed down from time immemorial, that an attack of influenza is most dangerous in the tuberculous, and that when a fatal issue is averted, the pulmonary condition is very frequently aggravated so that a closed case may become opened, an arrested lesion active, and an active case progressive.

B. Stivelman,<sup>4</sup> Medical Superintendent of the Montefiore Country Home Sanatorium, at Bedford Hills, New

(4) New York Med. Jour., July 5, 1919.

York, has summarized his experience with the effects of influenza on pulmonary tuberculosis as follows:

The epidemic of influenza appeared at the sanatorium several weeks later than at New York City, which is forty miles south, and only forty-eight hours later than in the nearest village, a half mile from the institution.

Tuberculous and non-tuberculous subjects seem to have been equally susceptible to influenza, the incidence in each case being 24 per cent.

Early and advanced cases were equally affected.

Pneumonic consolidations occurred as frequently in the non-tuberculous as in the tuberculous.

There was a mortality of 11.4 per cent, due to the epidemic.

Careful observation for four months, and re-examination of all patients so affected at the end of this period, showed that all the patients but two were none the worse for their experience, their general condition being as good as might have been expected normally.

So far, there seems to be no increase in the number of tuberculous patients seeking admission to the sanatorium, as a result of influenza, and more cases are erroneously sent for treatment on account of basal lesions than in corresponding periods of the past two years.

**Purulent Pneumococcus Meningitis in Influenza.** E. Doubourg<sup>5</sup> records six fatal cases of this kind, which occurred among soldiers of the French Army of the East at Salonica. The relative frequency of purulent meningitis as a complication of influenza in the army in the East, as compared with its rarity in France is attributed by Doubourg to the large proportion of native soldiers, and to the preponderating rôle of the pneumococcus in the complications of influenza. The black races are peculiarly susceptible to pneumococcus infections, and of the six cases reported, only one occurred in a Frenchman; the others were in negroes or natives of Madagascar. In Doubourg's cases, the pneumococcus was frequently associated in the sputum with the pneumobacillus, enterococcus *Micrococcus catarrhalis*, and Pfeiffer's bacillus. It was more frequently found in pure cultures in the fluid withdrawn by puncture of the lung, and was almost

(5) Gaz. hebdomadaire de médecine et de chirurgie, Dec. 14, 1919.

the exclusive factor in purulent pericardial and pleural complications. In nine cases of purulent pleurisy, eight were found to be due to the pneumococcus, and only one to a hemolytic streptococcus. Blood culture was made in thirty-four cases and yielded eight positive results, the pneumococcus being found in seven cases and the enterococcus in only one. Postmortem examination in six cases showed that the accessory sinuses and ear were always intact, so that the meningitis was due to speticemia and not to propagation. In most of the cases the onset of the meningeal symptoms was very sudden and death was never later than four days after the appearance of the first symptoms. In one case it occurred in a few hours after onset. One form of pneumococcus meningitis is manifested by attacks of acute delirium and homicidal impulses. The temperature chart is not characteristic. Cases with sudden onset usually terminate by hyperpyrexia, but occasionally the fever is not high, and the meningeal symptoms set in without much rise of temperature. All treatment so far employed has been unsuccessful. The best course to pursue is to prevent, if possible, the development of meningeal complications by the use of antipneumococcus serum, either subcutaneously or intravenously, in any severe case of pneumococcus infection, especially during an epidemic.

[Except for Type I there is no available antipneumococcus serum of real value.—B.]

**Influenzal Encephalitis.** G. Neve<sup>6</sup> has observed six cases of encephalitis in conjunction with, or soon after, an attack of influenza. One of his patients was a butcher, aged 46, whose family suffered from influenza. He was also "out of sorts" and lost appetite, but did not at once go to bed. After a few days he felt very ill, tired, and restless, with a sense of pressure in the head. On his admission to hospital a week after the development of symptoms, he seemed very debilitated, and movements were sluggish. He could hardly move his head, but his neck was not painful. The pupils were contracted; reaction to light was slow, and reaction to accommodation almost absent. He collapsed, sometimes to the right, sometimes to the left, when Romberg's

(6) Hospitalstid., Nov. 12, 1919.



test was made. He was drowsy, and complained of feeling heavy and giddy. He could read only for a short time, and for some days he complained of pain in the back of his head. When he was discharged from hospital, about six weeks after admission, his symptoms had vanished and the pupils reacted to light. Neve, who gives details of all his cases, found the clinical picture strikingly uniform, the differences noted being a matter of degree only. Every patient treated in hospital was given hexamethylenetetramine, and the recovery of all the patients was probably the result, in part, at least, of this treatment. [This statement is unjustified because the drug has no specific value as a bactericide.—B.] The most prominent symptoms were drowsiness, spasm or rigidity of certain muscles, nystagmus, diplopia, and paresis or paralysis of the iris. Only in one case was the interval between the influenza and the encephalitis as long as two months; this case, which was particularly severe, was thought to be one of reinfection with influenza.

**Influenza Prophylaxis.** H. Sahli<sup>7</sup> thinks that influenza spreads by direct contagion chiefly from droplets thrown off during speaking, coughing, etc. His assistant Dr. Lauterberg found by experiment that all commercial forms of masks used to prevent droplet infection were useless on those about the patients. Slightly better results were attained if the patient was masked which was very difficult to accomplish, as it interfered too much with breathing, and with the feeding of the patient. The author feels that the present status of influenza vaccination is in the experimental state and no positive results are determinable.

**Influenzal Paralysis of the Soft Palate.** G. Kickhefeld<sup>8</sup> has observed four cases of partial paralysis of the soft palate after a typical attack of influenza. The first case was that of a woman, aged 33, who in October, 1918, developed high fever which lasted three weeks. Her head and limbs ached, and she suffered from severe cough and much catarrh of the throat, but she was not attended by a physician. After the temperature had

(7) Cor-Bl. f. Schweiz. Aertze., February, 1919.

(8) Berlin. klin. Wochschr., Oct. 13, 1919.

fallen, her speech became nasal and slurred. On examination in hospital on Jan. 16, 1919, the movements of the soft palate were seen to be slow on both sides, and the occlusion of the rhinopharynx by the palate was incomplete. There was, however, no regurgitation of liquids by the nose. The quality of the voice was abnormally affected by closure of the nostrils (Gutzmann's test).

After giving details of his other cases, the author notes that the febrile illness preceding the paralysis of the soft palate was invariably characteristic of influenza: pain in the limbs, violent headache, great lassitude, pain in the eyes, and catarrh of the respiratory tract were uniformly present. All the patients denied the existence of a membranous deposit in the throat, of dysphagia or swelling of the cervical glands. Diphtheria, therefore, could be excluded. The paralysis was only partial in these cases, the subsequent course of which the author does not record. He remarks, however, that such cases often clear up spontaneously, and that when this does not occur the persistence of the symptoms may be due to functional disturbances having succeeded an organic lesion.

A. Peyser<sup>11</sup> expresses doubts as to the existence of a genuine influenzal paralysis of the soft palate, suggesting that undetected diphtheria might account for a proportion, at any rate, of the cases labeled as influenzal. In support of this view, he has recorded a case of paralysis of the soft palate with a recent history of influenza but not of diphtheria. He was about to demonstrate it as one of influenzal origin when he saw another case in which there was no history of diphtheria. However, when the discharge from the right ear was examined typical diphtheria bacilli were found. Finder's experience, recorded in the same journal, also points to a diphtheritic origin of the so-called influenzal paralysis of the soft palate. One of his patients was a married woman, who complained that she had not been able to speak properly since a recent attack of influenza. Paralysis of the soft palate was diagnosed, and, as she declared at first that she had not suffered from a sore

<sup>11</sup>90 Berlin. Klin. Wochschr., Oct. 13, 1919.

throat, but only from such characteristic influenzal symptoms as fever and pains in the limbs, the existence of diphtheria seemed improbable. But on further investigation it transpired that she had experienced some difficulty in swallowing, and when a bacteriologic examination was made diphtheria bacilli were found.

## COLDS

**The Etiology and Treatment of Colds.** This subject, though frequently looked upon as very commonplace, is one which confronts every man who practices medicine, and its discussion by O. T. Osborne,<sup>10</sup> of the Yale University School of Medicine will be welcomed.

He says first that while congestions of the mucous membranes of the upper air passages may simulate colds, probably all so-called colds are due to infection. Also, colds are contagious, and are disseminated by spraying the atmosphere when sneezing and coughing without proper protection. In families probably most colds are spread by closer contact, as by kissing, using the same drinking glasses and the same towels and, even more carelessly, by mothers using the same handkerchiefs for more than one child and for themselves. Those who have colds frequently have them from re-infection from themselves; and, doubtless many carriers of these germs may infect others.

The germs that produce colds are perhaps many. The *Micrococcus catarrhalis* and the *Bacillus influenzae* have been identified as the cause of colds and influenza. It has not been shown that the various types of pneumococci often found in the mouth can cause acute inflammation, or colds, of the upper air passages. Neither has it been shown that the various streptococci found in throats and noses cause so-called colds.

The deadly *Streptococcus viridans* does not cause colds, although this germ is often present in infection of the teeth and tonsils. Therefore, it seems hardly probable that the *Micrococcus catarrhalis* is the cause of all common colds. Evidently, there are other germs

---

(10) New York Med. Jour., March 29, 1919.

which rapidly spread contagion which have not yet been discovered.

As to vaccines, Osborne says that the injection of mixed bacteria found in the mouth and nose probably rarely prevents colds. It is to be noted that when patients receive such vaccines, they have also received general advice and have had some special nose and throat treatment that would tend to prevent the occurrence of colds. He emphasizes the fact that any infection of the upper respiratory tract should be considered as important and properly cared for. A cold always necessitates recuperation and always predisposes to another cold, and possibly, also to such infections as measles, whooping cough and scarlet fever in children.

Regarding prevention of colds, he says that if a child has adenoids that are in the least obstructive, they should be completely removed. Tonsils enlarged, but not large enough to obstruct the throat, in a child may at least be tolerated for a time, and not necessarily be immediately removed. If one or both tonsils are diseased, having pockets that harbor secretions, germs, and perhaps pus, there can be no question of the advisability of their immediate and complete removal. There can be no doubt that too many faucial tonsils are removed but, on the other hand, if the patient has recurrent attacks of tonsillitis, and certainly if he has had one or more attacks of acute rheumatism, the tonsils should be sacrificed immediately.

Also, there can be no half-way measure with either acute or chronic inflammation of one of the sinuses above the nose or of an ear. No measure should be left untried until the inflammation has abated and the germs of the disease have been eradicated. Nasal hypertrophies, or bone blocking of the nostrils must be conservatively treated. Minor operations in this region are more satisfactory than major and more dangerous resections. Chronic pharyngitis and recurrent subacute attacks of pharyngitis are frequently cured by causing normal breathing through the nostrils. It is to be remembered, also, that a neglected, decayed tooth, may harbor germs of infection in childhood as well as in adult life. In the adult, chronic infections of the teeth

and gums frequently harbor germs of the character that allow recurrent colds. Many cases of hay fever and asthma are first developed after frequent colds, even if specific irritants can later be found.

Besides these local measures of prevention the proper amount of fresh air during inside work in the day time, and during sleep is essential to prevent congestion of the mucus membranes of the upper air passages. The term "proper amount" is decidedly emphasized. The person whose enthusiasm for fresh air leads to exposure, to draft and chill, and who remains healthy in spite of these conditions, is not recognized as knowing how to protect himself. The factor of proper clothing is also as important. The clothing of the babe, the child, the youth and the adult should be sensible. The skin should always be comfortably warm and normal, especially in cold weather, and insensible perspiration should not be prevented. On the other hand, any clothing that causes profuse perspiration and over-heating of the body is deplorable. Such over-clothing predisposes to colds. Cold sponging or showers and morning sponging of the throat and chest with cold water are heartily recommended. Open-air exercise has its definite advantage; however, cold morning baths and much physical exercise, without proper training or proper grading of such exercise, is often a disadvantage to an individual and may even predispose to colds.

Under the heading of proper food, Osborne points out that abstinence from too much meat, from all stimulants and alcohol, from over-smoking and the avoidance of constipation are important items in protection against colds.

The pathology of colds is simply the various stages of inflammation of the mucus membranes. First, dryness, with congestion and swelling, later, an outpouring of mucus secretions with increased leukocytes and, finally, more or less purulent secretions. The local symptoms are well known.

In the early stages, a cold can frequently be avoided. Of primary importance in this treatment is a brisk cathartic, a milk and cereal diet, and a greatly restricted intake of fluids. Also, 1/500 grain of atropine sulphate



should be given to an adult every two hours for five doses, and then every three hours for five more doses. A child 10 years old could have this dose every three hours for five doses, and then every six hours for five more doses. The throat and mouth may be washed with a mild alkaline wash; Osborne considers nasal sprays inadvisable at this stage. Hot baths, body-baking, and electric-light baths, if one has the opportunity to take such treatment, by bringing the blood to the surface of the body, and then relieving the congestion in the nose and throat may aid in avoiding a cold. If there is much fever, a dose of antipyrene may be advisable.

If a cold continues to a more productive stage than is seen in the first days, the object of the treatment is to hasten the secretion or excretion. Atropine should be stopped and ammonium chloride given in syrup or citric acid and water. If there is an irritable cough, codeine may be added to this mixture. If the patient has severe backache, headache, and more or less fever, one or two small doses of acetanilide may be given or acetyl salicylic acid may be given in two or three doses. These drugs should be continued two or three days, and the patient should remain in bed for an equal length of time.

If the cough becomes productive and not irritable, the ammonium chloride mixture may be continued, but without the codeine. If the expectoration is profuse, terpine hydrate may be substituted for the ammonium chloride. It should be given in powder or in capsule, or if a tablet is given, it should be crushed before swallowing. If the patient has difficulty in raising the mucopurulent secretion from the bronchial tubes, and it is sticky and hard to expectorate, sodium iodide in small doses is the best treatment. After any cold, the patient requires a tonic, such as a capsule of quinine 0.10 gram, reduced iron 0.05 gram, and strychnine sulphate 0.0015 gram, three times a day, after meals. If there is any congestion of the ears, the quinine should be omitted. Some liquid bitter tonic may be given if it seems preferable.

## PNEUMONIA

**Biochemical Studies of Pneumonic Exudates.** While the work upon which this article is based is of a highly technical nature, the results obtained by it are of importance to an understanding of pneumonia and the way in which its results are brought about. A preceding article dealing with this same subject has brought out the following properties of pneumonic lung exudates. The investigations included in the present article were made by Charles Weiss<sup>1</sup> alone, and they deal with further biologic and chemical analyses of toxic substances in pneumonic exudates. These exudates were obtained from human lungs in the stage of gray hepatization and the studies were conducted by the method of anaphylactic-sensitization and intoxication of guinea-pigs with various proteins derived from normal and pneumonic lungs, exudates, serums, etc.

The summary of observations made is presented as given by the author as follows:

Salt solution extracts of human lungs in the stage of gray hepatization in pneumococcus lobar pneumonia are more toxic for experimental animals than similar extracts of normal lung tissue. The method of extraction influences the toxicity of both extracts.

Lethal doses of extracts of both pneumonic and normal lung tissue injected intravenously usually produce anaphylactic-like symptoms.

Sterile extracts of pneumonic lung tissue of dogs removed forty-eight hours after intrabronchial insufflation of virulent pneumococci are more toxic than similar extracts of consolidated lung following intrabronchial insufflation of sterile aureolat in suspension, and both of these are somewhat more toxic than extracts of equal weights of normal dog lung.

The toxicity of extracts of normal and pneumonic lung is decreased by heating, drying and filtration through porcelain filters.

Extracts of human pneumonic lungs in gray hepatization are hemolytic for guinea-pig cells, whereas similar extracts of normal human and dog lungs and of con-

(1) Archiv. Int. Med., March, 1919.

solidated dog lungs following the intrabronchial insufflation of virulent pneumococci and sterile aleuronat, are generally non-toxic, i.e. The hemolytic activity of these extracts is neutralized by horse antipneumococcus serum as well as by normal rabbit serum; it is reduced by heating and drying and usually completely removed by porcelain filtration.

Extracts of human pneumonic lung in gray hepatization inhibit the agglutinating activity of antipneumococcus serum.

The present investigations deal with further biologic and chemical analyses of toxic substances in pneumonic exudates. They consist of biochemical studies of pneumonic exudates obtained from human lungs in the stage of gray hepatization by the method of anaphylactic sensitization and intoxication of guinea-pigs, with various proteins derived from normal and pneumonic lungs, exudates, serums, etc. The following observations were made:

Pneumonic exudates contain at least two toxic proteins: (1) a specific sensitization protein apparently identical with the pneumotoxin which is liberated on the dissolution of virulent pneumococci and (2) an extremely toxic, pyrogenic albumose.

There are also present normal serum proteins: serum albumin and serum globulin, leukocytes, and fibrin.

Neither digested pneumococcus protein nor albumin derived from the lung tissue, possessing sensitizing powers, are demonstrable.

The globulin fraction of human pneumonic exudate is non-toxic and identical with similar normal globulin.

The albumin fraction of pneumonic exudate is toxic and possesses marked specificity. This is ascribed to the digestive action of the enzymes of the exudate.

The albumose fraction is far more toxic. Dyspnea, convulsions and death follow the intraperitoneal injection into white rats of doses of 1 gm. per kilogram. Intrathoracic injection into rabbits of doses of 0.02 gm. per kilogram produces a rise in temperature, dyspnea, a hemorrhagic extravasation into the alveoli of the lung, and an acute diffuse nephritis. On repeated intraperi-

toneal injections of this albumose into rats, a tolerance to it can be established.

Large amounts of ether-soluble, non-toxic, hemolysis-inhibiting substances were extracted from pneumonic lungs. These are assumed to have the power of neutralizing the hemolytic activity of the pneumotoxin *in vivo*.

The formation of the exudate in pneumonia is considered by Weiss to be in part due to increased permeability of the endothelial cells of the lung for various normal serum albumins, globulins, fibrinogen and enzymes as the result of the injury exerted by the pneumotoxin on their cement substances. The toxin is also regarded as a lymphagogue. It hinders the autolysis of the exudate and the favorable action of antipneumococcus immune bodies and thus produces toxic autolysis-inhibiting, pyrogenic albumoses. With the development of excess amounts of specific antibodies, of bactericidal and phagocytic substances, and of a tolerance to the toxic albumoses, the deleterious influences of the toxins and albumoses are neutralized. Autolysis of the exudate is now unhindered and the products are non-toxic amino-acids. The equilibrium of this system being governed by the laws of mass action, the change from febrile toxemia to the afebrile, atoxic state is necessarily an abrupt one—crisis.

**Antemortem and Postmortem Bacteriology of Pneumonia.** This antemortem and postmortem study of the bacteriology of pneumonia was carried by E. G. Birge and L. C. Havens,<sup>2</sup> at Camp Wadsworth, S. C.

The paper is confined entirely to the bacteriologic results obtained postmortem from 124 cases and antemortem from the sputum of sixty of these cases.

The results obtained impress the authors as being important for several reasons. The results antemortem were checked by findings postmortem, so that it was possible to determine the infective agent in the lung itself. It was also possible to determine the real value of the present methods of "typing" pneumonia from the sputum.

---

(2) New York Med. Jour., March 29, 1919.

The technique in determining the predominating organism at autopsy and from the sputum was the same, so that the results are comparable. The typing was done by the Avery method and by the inoculation of mice.

The results obtained are extensively tabulated and from them it is concluded that the *Streptococcus hemolyticus* was an important factor both as a primary and secondary agent.

The *Bacillus influenzae* was found, but only under conditions which lead to doubt as to its being the cause of the primary infection.

The evidence at hand points to the fact that Type III pneumococcus is found in healthy carriers, and this fact can not account for the number of cases of pneumonia caused by this organism.

The prevalence of Type IV pneumococci recovered from the sputum leads to the belief that all such cases should be looked on with suspicion unless confirmed by very carefully collected specimens or an autopsy.

In prolonged cases, those extending well over a week, the disagreement in bacteriologic findings antemortem and postmortem makes it apparent that repeated sputum examinations are desirable in order to follow intelligently the changing condition of the infection.

**Meningococcus Pneumonia.** The occurrence of post-influenzal pneumonia in which *Diplococcus intracellularis meningitidis* was isolated has been observed and recorded by M. L. Holm, and W. C. Davison.<sup>3</sup>

These observations were made at Camp Coetquidon, A. E. F., France. Prior to the epidemic of influenza, there were no instances of meningococcus meningitis in the hospital where these authors were working. It is brought out in the article that coincident with the occurrence of meningococcus meningitidis pneumonia there occurred a considerable number of meningococcus meningitis cases.

The presence of influenza at this Camp was first noted about Sept. 1, 1918, and many cases of pneumonia developed. On Sept. 3, 1918, bacteriologic cultures of the lungs at autopsy on a case of pneumonia showed a pure growth of meningococci (Type A Pasteur). About two

(3) Bull. Johns Hopkins Hosp., November, 1919.



weeks later, meningococci were recovered from the sputum in two pneumonia patients. Following this cultures were taken from the throats of all respiratory patients in the hospital. Among 114 thus cultured meningococci (Type B Pasteur) were isolated from seven patients, six of whom had pneumonia. Throat and sputum cultures of meningococci were recovered from twelve additional cases of pneumonia.

During the period studied, seventy-eight cases of pneumonia came to autopsy. Meningococci were recovered from the lung tissue in a total of twenty-three instances; in pure culture in seven and in mixed culture in sixteen. The majority of the meningococci isolated were Pasteur Type B and were also agglutinated by Gordon's meningococcus sera, Types 2 and 4 (corresponding to the Rockefeller Institute normal meningococcus).

From a bacteriologic study of the patients who had meningococcus meningitis, of which twenty-two cases occurred during this period, blood cultures were taken in sixteen, with three positive results. Positive results were all obtained from early cases, and no positive blood cultures were obtained after the first days of the disease. In one case the spinal fluid was clear at the time the positive blood culture was secured. In this culture the meningococci numbered 2 per c. c., yet on the following day when the spinal fluid showed a high cell count, numerous meningococci, a second blood culture gave negative results. Spinal fluid cultures all gave positive results at the time the first turbid fluid was secured. In nearly all instances, however, cultures failed to grow the meningococci after the third or fourth days, even though the white cell count remained high for a much longer period.

Panophthalmitis developed in one instance and meningococci were recovered from the eye after enucleation.

A study of meningococcus carriers was made during the progress of the epidemic. The results obtained are indicated in the following table.

Time	Number of Men Carriers		Per- centages
	cultured	found	
Sept. 20, 1918.....	1,160	198	16
Oct. 20, 1918.....	2,286	280	12
Dec. 6, 1918.....	1,254	110	8
Feb. 10, 1919.....	1,196	60	5

The greatest number of carriers was generally found present in the barracks where respiratory affections were most numerous.

In discussion it is pointed out that meningococci ranked third among the bacteria found most frequently in the lungs at autopsy in cases of pneumonia, being exceeded only by pneumococci and *B. influenzae*. However, if cerebrospinal meningitis cases be included, the meningococcus becomes the most frequently found organism in the lesions causing death during the epidemic. Out of fifty strains of meningococci typed from carriers selected at random, forty-four were Type B, four Type C, and two Type A Pasteur. Eighteen cases of cerebrospinal meningitis were caused by Type B, meningococcus. Nineteen autopsy cultures from cases of meningococcus pneumonia showed fourteen Type B, three Type A, two C, Pasteur. It is, therefore, evident that the prevailing type of meningococcus during this period was Type B Pasteur and was responsible for all of the meningitis cases as well as the larger proportion of meningococcus pneumonia cases. The frequent association of meningococci with *B. influenzae* is of special interest. On artificial media, the two organisms grow together exceedingly well. The possibility of a symbiotic pathogenicity of these organisms is worthy of further study.

A continuation of the work of Holm and Davison described in the preceding article consists of a bacteriologic examination of contacts of meningococcus pneumonia and meningococcus meningitis cases during the latter part of September and the early part of October, 1918, at Camp Coetquidon A. E. F. France.

In order to determine whether the incidence of these cases was due to contact or infection in the hospital or in the barracks, cultures from the rhinopharynx were taken: (1) from every new patient at the time he was received into the hospital; (2) from all patients and at-

tendants in the hospital; (3) from all patients at the time of their discharge from the hospital; and (4) from all contacts of recent cases of meningococcus meningitis in the barracks.

The conclusion reached in the preceding article is further substantiated by the results obtained in the present work, which was carried out by W. C. Davison, M. L. Holm, and V. B. Emmons.<sup>4</sup> The results obtained in this work are indicated in the accompanying table:

Situation of men examined	Number of men cultured	Number found positive <i>i. e.</i> , with meningococci in the rhinopharynx	Percentage of positive or carrier rate
Receiving wards.....	102	8	8 per cent.
Other hospital wards .....	456	32	7 per cent.
Discharged patients .....	596	85	14 per cent.
Contacts in barracks, 141st Field Artillery .....	261	38	14 per cent.
Contacts in barracks, 142nd Field Artillery .....	86	8	9 per cent.
Contacts in barracks of 114th Trench Mortar Battery ...	66	13	20 per cent.
Contacts in barracks of 114th Ammunition Train .....	6	0	0 per cent.
Total .....	1573	184 *	12 per cent.

\* The great majority of these carriers were of the temporary class. Of 152 meningococcus carriers cultured on the third day only thirty-seven were positive. Of 160 carriers at the next examination the sixth day only fifteen were positive.

To the authors it was evident that the meningococcus was both endemically and epidemically distributed in the rhinopharynges of the troops of Camp Coetquidon and that this explained the relatively large number of cases of post-influenzal pneumonia in which meningococci were isolated.

**Pneumonia and Some of its Complications.** This report by J. C. Greenway, C. Boettiger and H. S. Colwell<sup>5</sup> is based upon the study of 2,344 patients suffering with pneumonia, and its various complications at the Base Hospital at Camp Bowie, during the period from

(4) Bull. Johns Hopkins Hosp., November, 1919.

(5) Archiv. Int. Med., July, 1919.

September, 1917, to January, 1919. During the first part of this time, that is from Sept. 1, 1917, to Jan. 1, 1918, there was in this camp an epidemic of measles, at which time 3,624 patients contracted the disease, and of these, a large number developed pneumonia, many of whom suffered also numerous serious complications: there was a high death-rate.

In addition to the measles there was a widespread infection of the upper respiratory tracts throughout the camp. There were 973 cases of pneumonia, and in only 363 of these could there be obtained a history of measles within a month preceding the development of the pneumonia. Of the patients who developed pneumonia 237 died, giving a mortality of 24.4 per cent. Of those patients with pneumonia 17 per cent. developed empyema, and among these, there was a mortality of 32.5 per cent. The prevalence of infection with hemolytic streptococci was shown by a high incidence of the organism in the pleural fluid and in direct lung cultures.

During the period from Jan. 1 to Sept. 27, 1918, there were 538 patients who suffered with pneumonia, and only forty-eight of these gave a history of an antecedent infection within a month. In the majority of instances, there was a definite history of exposure, insufficient clothing or over-heating followed by injudicious cooling which may have been a precipitating factor in the onset. The total mortality for this period was 7.4 per cent., there being forty fatalities among the 538 cases. Fifty-two patients (9.7 per cent.) developed empyema and provided 37.5 per cent. of the total deaths.

In all the lobar pneumonia patients pneumococci were found in the sputum, and ten of the eighteen fatal cases reacted to specific type serum I and II. Hemolytic streptococci were still an important factor and in three of nine purulent pleurisies this organism was present in addition to the pneumococcus.

From Sept. 17, 1918, to Nov. 15, 1918, 3,876 patients developed the infection that was designated as influenza, and were admitted to the Base Hospital. Taking white corpuscle blood counts on these patients it was found that the largest number of counts was below 10,000; as the severity of the epidemic declined, the total white

counts were higher, and also the polynuclear percentages were correspondingly increased. Leukopenia, that is a count under 5,000, was not a common finding, though absence of leukocytosis was the rule.

It is notable that among the white men 252 per thousand who were exposed developed the infection; 114 per thousand developed pneumonia. Among the 795 cases of pneumonia the history of influenza within the preceding month was obtained in 728. No deaths were attributable to uncomplicated influenza. There was noted a higher morbidity rate for influenza and pneumonia among the black troops, but the mortality percentage, 17.1 per cent., among them was somewhat less than that of the white troops, 20.8 per cent.

A bacterial study of the nasopharyngeal secretions from patients with influenza yielded hemolytic streptococci 45 per cent.; pneumococci, type undetermined, 3.5 per cent.; influenza bacilli present, 0 per cent.; non-hemolytic streptococci, 10 per cent.

A bacteriologic study of materials removed at post-mortem examination of bodies was made. In this work it was found that the group showing the interstitial type of pneumonia and the highest proportion of complications showed hemolytic streptococcus in 64 per cent. of lung cultures. Influenza bacilli were found in 16 per cent. of the remaining bronchopneumonia and in 25 per cent. of the lobar pneumonia, but were always associated with other organisms. In all the lobar pneumonia patients the pneumococcus was found.

The onset of pneumonia in the patients seen during and following the measles epidemic in 1917 was observed to be late, that is, several weeks after the upper respiratory tract infection had occurred. During the influenza epidemic in 1918, the pneumonia developed within a few days, or coincident with the first symptoms of the respiratory tract infection.

By a study of the lobes involved in the pneumonic process, it was found that of 1,536 cases in which the first involvement noted affected only one lobe, the right lower lobe was involved first in 211 cases, the left lower lobe in 679 cases, the right upper lobe in fifty-four and



the left upper lobe in forty-eight and the right middle lobe in forty-one.

In a large number of instances of pneumonia associated with the influenza epidemic, the initial involvement was simultaneous in both lower lobes.

The authors say that of 254 satisfactory blood cultures of patients taken during life, thirty-five, or 13.8 per cent. were positive. Of the 219 cases in which sterile blood cultures were obtained, twenty-four or 11 per cent. of the patients died, whereas in the thirty-five cases of positive blood cultures, fourteen patients or 40 per cent. died. This is in accord with the views that a positive blood culture during life makes the prognosis grave.

In the treatment of pneumonia, specific serum was used in all Type I cases, except those which had practically defervesced at the time of type determination.

There were, during 1918, 142 Type I infections. One hundred and twenty-five of these patients were treated with serum, seven died, a mortality of 5.6 per cent. Four of these seven deaths were charged to pneumonia, and really were caused by empyema. Seventeen Type I infections were untreated. None of these patients died. The untreated patients were for the most part those who because of the mildness of their infection or delay in being sent in to the hospital had their crisis before the type of the infection could be determined. No serious results followed the administration of serum, and from their work these authors state that the earlier it is used the more striking the results obtained.

All patients received digitalis in large doses as soon as the diagnosis was made. Other forms of treatment were symptomatic.

Of the complications encountered empyema was by all means the most prominent. The incidence of empyema was highest among the pneumonias following measles. For the entire period cases complicated with empyema constituted 10.6 per cent. of the total pneumonias and furnished 25.6 per cent. of the total pneumonia deaths.

The appearance of the pleural exudates caused by the *Streptococcus hemolyticus* was characteristic. Repeated aspiration of such fluid followed by operation after the

acute pneumonitis had subsided gave a most satisfactory result in this work.

The occurrence of encapsulated pus was very common, especially in the streptococcus infection. These pockets were frequently multiple and offered great difficulties from an operative standpoint.

**Prophylactic Vaccination Against Pneumonia.** The work of Cecil and Austin in using prophylactic vaccination against pneumonia has furnished considerable evidence that vaccination against Types I, II and III pneumococci is practical and that it affords satisfactory protection against the pneumonia produced by these types. In view of the widespread prevalence of pneumonia in the American Army, especially in the encampments, it was obvious that immediate effort should be made toward instituting a more extensive trial of pneumococcus vaccine and, if the results justified it, the establishment of pneumonia vaccination on an efficient and permanent basis.

It was with this idea in mind that Russell I. Cecil and Henry F. Vaughan<sup>6</sup> were detailed to Camp Wheeler for the purpose of using prophylactic pneumococcus vaccine on soldiers at that camp.

They state that following the work with typhoid lipovaccine, experiments were undertaken at the Army Medical School with pneumococcus lipovaccine, and here again it was found that pneumococcus vaccine in oil produced good immune reactions and that large doses could be administered without ill effects. It was therefore decided to prepare, in addition to the typhoid lipovaccine, a pneumococcus lipovaccine of Types I, II and III, and to supply it to the Army for vaccination of volunteers. This work was carried out by the authors at Camp Wheeler, where 13,460 men, or about 80 per cent. of the entire camp strength were vaccinated against pneumonia with pneumococcus lipovaccine.

The dosage employed in all cases was 1 c. c. of the lipovaccine containing approximately 10 billion each of pneumococcus Types I, II and III.

Both the local and general reactions produced by the vaccine were usually mild. Only 0.7 per cent. of those

---

(6) Jour. Exper. Med., May, 1919.

who received the vaccine were sufficiently affected to need hospital care. None of these was seriously ill, and a majority returned to duty on the second or third day after admission.

Most of the troops inoculated were under observation for two or three months after vaccination. During this period there were thirty-two cases of pneumococcus Types I, II and III pneumonia among the vaccinated four-fifths of camp, and forty-two cases of pneumonia of these types among the unvaccinated one-fifth of camp. If, however, all cases of pneumonia that developed within one week after vaccination are excluded from the vaccinated group, there remain only eight cases of pneumonia produced by fixed types, and these were all secondary to severe attacks of influenza. This exclusion is justified by the fact that protective bodies do not begin to appear in the serum until the eighth day after injection of pneumococcus lipovaccine.

There is no evidence whatever that pneumococcus vaccine predisposes the individual even temporarily toward either pneumococcus or streptococcus pneumonia.

The weekly incidence rate for pneumonia (all types) among the vaccinated troops was conspicuously lower than that for the unvaccinated troops.

The pneumonia incidence rate per 1,000 men during the period of the experiment was twice as high for unvaccinated recruits as for vaccinated recruits, and nearly seven times as high for unvaccinated seasoned men as for vaccinated seasoned men.

Influenza causes a marked reduction in resistance to pneumonia even among vaccinated men. Of the 155 cases of pneumonia (all types) developing one week or more after vaccinations, 133 were secondary to influenza.

The death-rate for 155 cases of pneumonia (all types) that developed among vaccinated men one week or more after vaccination was only 12.2 per cent., whereas the death-rate for 327 cases of all types that occurred among unvaccinated troops was 22.3 per cent. The death-rate for primary pneumonia among vaccinated troops was 11.9 per cent. Among unvaccinated, it was 31.8 per cent., almost three times as great. On the other hand, the mortality rate in pneumonia secondary to influenza

is about the same for the vaccinated and unvaccinated groups.

In conclusion, it must be admitted that the results of pneumococcus vaccination at Camp Wheeler have not been so striking as those obtained at Camp Upton in 1918, largely on account of the influenza epidemic; but although influenza obscured to some extent the effect of pneumococcus vaccination at Camp Wheeler, the results are sufficiently encouraging to justify its further application in civil as well as in military life.

**Treatment of Pneumonia.** This discussion of the treatment of pneumonia is a clear comparison of two distinct methods that were carried out at Camp Wheeler, with brief discussion of the results obtained by each method. The article is written by George W. Head,<sup>7</sup> of Minneapolis, who states that an epidemic of pneumonia began at Camp Wheeler about Oct. 5, 1918, and continued through the months of October, November, December, and part of January, 1919. It appeared coincidentally with an epidemic of influenza which swept through the Camp at that time.

As two radically different methods were employed in the treatment of the patients during this epidemic, a study of the results offers a useful field of observation and some helpful suggestions. Comparison between these two methods is considered fair, first, because the epidemic was continuous during the time this study was made; second, the same disease, namely, influenza, and no other, was prevalent and active as the underlying causal factor. Third, the same type of pneumonia pathologically was about equally distributed between the two groups.

The method of management from Oct. 5 to Nov. 24, 1918, was the so-called open air or open ward treatment. It can be thus summarized:

All the windows and doors in the ward were to be kept open day and night. Rain, cold winds and damp night air were no contradiction of the order.

No screens or blankets were to be hung up at the windows or placed before the doors to prevent the free circulation of air in the wards.

(7) Jour. Amer. Med. Ass'n, May 3, 1919.

Soldiers in the wards were encouraged to keep their heads close to the windows and lie so that the cold air sweeping in from the outside could be better breathed in. If a soldier complained of a cold draft of air on his head, he was told it was good for him; that the fresh air would make him well.

No cotton jackets or chest protectors were to be used. The patients were to be well supplied with blankets.

Ward fires were to be allowed to go out at night. On cold, damp days the wards were always cold and chilly, because all windows and doors were open. Under the open ward or open air treatment (Group 1) 966 patients with acute pneumonia were cared for between Oct. 5 and Nov. 24, 1918, with 135 deaths, a mortality of 13.9 per cent. November 24, while the epidemic was at its height, a radical change in treatment was made, as follows:

All windows and doors in the wards were ordered closed and the patients guarded in every possible way from drafts of cold air, chilling and exposure.

All sick soldiers with pneumonia on outside porches were ordered moved into wards and cared for indoors where they were warm and comfortable.

Every soldier with pneumonia was provided with a cotton jacket to keep his chest warm and to protect it from drafts and currents of cold air.

Ward surgeons, nurses and corps boys were instructed to handle and care for their patients so as to avoid, at all costs, chilling. The bed clothing was to be kept tucked in. The arms were to be kept under the bed covers. Plenty of blankets were to be used on cold nights, etc.

Fires in the wards were ordered kept going day and night. Wards were to be kept free from a feeling of chill in the air. This could not always be done on cold days.

Special nurses were provided for the desperately ill.

Bathing was discouraged except for purposes of cleanliness, and then only when wards were warm. Attending medical officers were cautioned to avoid prolonged examinations and to protect the patients well from chilling while examinations were being made.

Under the closed ward treatment (Group 2 as outlined



in the foregoing), 435 patients with active pneumonia were cared for between Nov. 24, 1918 and Feb. 1, 1919, with fourteen deaths, a mortality of 3.2 per cent.

It is said in comment that the knowledge possessed relative to the lowered vital force created in the tissues of the body when those structures are subjected to chilling, and a consideration of the lowered cell resistance against invading organisms created by exposure to currents of cold air, make it unreasonable to accept the open ward treatment of pneumonia as the best form of management. Any clinician who has walked through long wards of soldiers desperately sick with pneumonia, every man lying with his head and chest next to an open window, through which on cold days and night, cold and often damp winds are blowing, who has seen these men with pinched blue faces, with cold hands and feet, has heard them again and again request that the windows and doors be closed to keep them from feeling chilly, can not help but be convinced that this form of management for sick patients in an acute disease like pneumonia, is unwise.

These patients must be kept warm and comfortable. Their skins must be red, not blue. They must feel warm, not cold. They must be cared for so as to be in a high state of febrile reaction with a high, full bounding pulse. Heat, not cold and chilling, produces this effect.

The study of these 1400 cases of pneumonia showing the low death-rate in the Group 2 cases, justifies this conclusion and points the way to the more successful management of this disease.

[While the conclusions made are rational, one should remember that open air treatment of pneumonia may be made in a way which will be a helpful measure and at the same time preserve the comfort and well being of the patient. Adequate protection of the body surface and head may be secured with proper and sufficient clothing. Then no matter how cold the respired air if pure it will enhance recovery.—B.]

**Type I Pneumonia Treated with Antipneumococcus Serum.** From Feb. 10 to March 12, 1919, 135 cases of pneumonia were admitted to the Base Hospital at Camp Upton, New York. Of this number, 50 per cent. or sixty-eight cases were diagnosed bacteriologically as

having Type 1 pneumococcus the predominating organism in their infection.

This small epidemic was practically confined to the colored troops, only four out of the sixty-eight cases affecting white men. These troops embarked from Brest, sailing to New York, and were then transferred to Camp Upton for demobilization. On entering the hospital they presented the picture of acute lobar pneumonia. The present article is published for the purpose of giving the results obtained by treating these lobar pneumonias that were produced by pneumococcus Type I with pneumococcus serum obtained from the Rockefeller Institute in New York. In the sputum typing of these cases, fifty-eight were found to yield Type I pneumococci only, while ten produced mixed cultures, but with Type I pneumococcus predominating, and were not different in any details from the patients who presented Type I pneumococcus only. Before treating the patients with serum, 0.5 c.c. of normal horse serum was given subcutaneously for desensitizing purposes. In only three instances was there an anaphylactic reaction, and these were slight. The serum was given at eight-hour intervals day and night until the rectal temperature registered 100° F. or lower, or evidence of complication or impending death made it advisable to stop the treatment. The dosage employed was 100 c.c. given intravenously, keeping the serum slightly warmer than the body temperature, and allowing it to flow in very slowly. A gravity bottle was used, this being connected with an intravenous needle by rubber tubing, around which were wrapped warm towels to keep the solution at the proper temperature. Of the sixty-eight patients, sixty-one received the serum. The least amount given to any one individual was 30 c.c., the largest amount 900 c.c. The total amount used was 20,955 c.c. or the average amount per patient of 344 c.c.

Of the sixty-one patients having the serum, thirty recovered by crisis, twenty-two by lysis, and nine died. To the thirty who recovered by crisis, the total amount of 8,665 c.c. was administered, or an average dose of 288 c.c. Those cases ending in lysis received a total amount of 9,010 c.c. or an average dose per individual of 410 c.c.

To those who died 3,200 c.c. were given, or an average dose per individual of 356 c.c.

In addition to the serum treatment, general treatment was carried out. Each patient had 1,000 cu. ft. of air space. The windows were open day and night, and on sunny days the patients were moved to the porch. Rather large doses of digitalis and whisky were used during the critical stage, and codeine was administered when a sedative was necessary.

The mortality in this group of patients was 14.7 per cent. This is higher than the rate expected by the Rockefeller Institute, namely, 7.5 per cent., but this higher death-rate might be explained by a lower resistance to pneumonia of the colored race, the unfavorable season of the year and the forced moving of troops from place to place.

The authors of this article, Charles F. Tenney and William T. Rivenburgh,<sup>8</sup> used Type I serum in two cases of pneumonia with positive blood cultures, one with *Streptococcus viridans*, and the other Type IV pneumococcus. Each patient received eight injections after which the blood cultures of both were sterile and both recovered. This was done in desperation because of the death of three patients with positive blood cultures developing prior to these two.

**The Use of Antipneumococcus Serum.** This article is based on a year's experience in the Presbyterian Hospital of New York City, and is published by T. S. Hart.<sup>9</sup> The observations were made upon thirty-three patients, the intention being to treat every one with serum as soon as it was definitely decided that the case belonged to the class of pneumonia produced by pneumococcus, Type I, without regard to the day of the disease or the apparent severity. Under these conditions, thirty-one patients received one or more intravenous injections of serum. One patient died before the grouping was definitely settled, another had so far recovered when the group was determined, that there was no object in serum administration. The method of administration followed as exactly

---

(8) Archiv. Int. Med., November, 1919.

(9) Med. Record, May 31, 1919.

as possible the rules laid down by the Rockefeller investigators.

From every patient showing on admission physical signs of pneumonia a blood culture was immediately secured and, when possible, a specimen of sputum. At the same time the sensitiveness to foreign protein was determined by the intradermal injection of 0.02 c.c. of sterile horse serum diluted with nine parts of normal salt solution. If the patient showed signs of sensitization, he was de-sensitized by subcutaneous injections of serum in the usual manner. As a result of these precautions two patients were found highly sensitive to horse serum. They were de-sensitized and showed no further reaction at the time of the administration of therapeutic doses.

A positive diagnosis of the group was obtained in eight hours in several instances. In others, it was delayed by the impossibility of obtaining a suitable specimen of sputum. This made it impossible to administer serum to six patients within twelve hours after admission and to nineteen patients within twenty-four hours after admission. The remainder of the group received the initial dose of serum more than twenty-four hours after admission.

An initial dose of from 90 to 100 c.c. of serum was given. If at succeeding eight hour periods, the temperature remained above  $102^{\circ}$  F., a like amount of serum was administered. A single dose of 100 c.c. was given in two cases, and the serum was then discontinued on account of the fall in temperature. In four instances, a total amount of 1000 c.c. was given to each patient: in three of these it was then discontinued on account of the fall in temperature. These patients recovered. The fourth patient showed no benefit and the administration was therefore stopped. He died some days later.

Early reactions occurred in fifteen cases immediately following the first dose of serum. Of these, seven were very insignificant. In eight cases the symptoms were more pronounced, extensive urticaria, dyspnea, cyanosis, acceleration of the pulse, sometimes cough, vomiting and headache. In none of these were the manifestations alarming, and they were at once relieved by the adminis-

tration of adrenalin. Reactions appeared in all but two patients who lived long enough to allow these to develop. They were classified as mild, ten; medium, six; severe, nine. These reactions usually appeared on the sixth or seventh day after the therapeutic injection of the serum.

One of the strongest arguments for the use of anti-pneumococcus serum has been its experimentally demonstrated power to render sterile the blood stream of animals infected with pneumococcus. The results obtained in this respect by the present work are analyzed and the author says that while the evidence is decidedly fragmentary, it seems to indicate that the administration of serum affords a definite aid to Nature's efforts to sterilize the blood stream. The failures which are recorded are very instructive. In each case there was a localized focus of infection which continued to furnish pneumococci to the blood stream. In one instance, this was an empyema. In three others, an acute endocarditis was present, and in two of these which were examined postmortem, there were found on the heart valve, fresh vegetations, containing pneumococci.

Seven of the patients treated with serum in this work died. From a careful consideration of these seven cases, it is evident that in nearly every one death was due to some lesion other than pneumonia. The administration of serum appeared to have little or no influence on these complications when once established.

In answer to the question as to whether or not the earlier administration would have prevented the development of these complications, Hart says that present evidences give no definite answer. He gives the following brief *résumé*:

A positive blood culture in lobar pneumonia is usually an indication that one may expect a severe course.

It is rare for a patient who has received serum to escape a subsequent "serum illness." This may be mild or severe, but bears no relationship to the amount of serum given. Serum illness in these cases does not endanger life.

Antipneumococcus serum is a distinct aid to Nature's effort to sterilize the blood stream.

When serum fails to sterilize the blood an acute pneu-



mucoccus endocarditis should be considered as a possible cause. This was present in three of the patients in this group.

**Serum Therapy of Lobar Pneumonia.** In this report of the treatment of lobar pneumonia with the antipneumococcus serum prepared by Kyes, John H. McClellan<sup>10</sup> includes only such cases as are beyond reasonable doubt frank pneumococcus lobar pneumonia. There were 323 such cases which came under observation at the base hospital at Camp Grant, Rockford, Ill., from Oct. 1, 1917, to Sept. 21, 1918. No case was reported as lobar pneumonia, or is here included, which did not show definite lobar consolidation as evidenced by tubular breathing, increased tactile fremitus, bronchophony and flatness.

The relative incidence of type of pneumonia is shown in the following table:

RELATIVE INCIDENCE OF TYPES OF PNEUMONIA

	Group				
	I	II	III	IV	Total
Number of cases.....	43	56	13	199	311
Percentage of cases.....	11.8	18.7	4.1	65.2	

Bacteriologic examination of the sputum from these patients, leukocyte count and other factors are discussed in detail.

In regard to the use of the serum, the author says that in the treatment of all cases, systematic use was made of a polyvalent antipneumococcus serum prepared at the University of Chicago by Dr. Preston Kyes. In view of the results obtained by the previous use of this serum in 115 cases of pneumonia in a civil hospital, Major Joseph A. Capps, chief of the medical service, introduced the use of the serum as a routine procedure at Camp Grant, Oct. 1, 1917, and the results obtained were such as to indicate its continued use. It must be borne in mind, of course, that clinical evidence as to the efficiency of any therapeutic reagent is at best indefinite and must be accumulated in great amount and under varied conditions before final conclusions may be drawn. However, in this fairly large series of cases, the serum appeared to modify the course of the disease in several particulars with such

(10) Jour. Amer. Med. Ass'n, June 28, 1919.

constancy that it is the conclusion of those observing its use that the low death-rate resulting should be interpreted as being in a considerable measure due to the therapeutic efficacy of the serum. In its action, the serum appears distinctly to reduce the toxemia, to reduce the general level of the temperature and especially that of the pulse. In most instances the leukocytosis is successively increased by injection of the serum; but this is not without exception. The impression is gained that in the large number of cases displaying a crisis on or before the fourth day, the sudden change bears a direct time relation to the injection of the serum.

The serum was employed for the most part intravenously, the usual dose being 2.5 c.c. once or twice daily. The total number of doses given varied from one to twelve with individual patients, in the average case from three to five injections being given. Of the 322 cases under consideration, twenty-five terminated fatally, the death rate being 7.7 per cent. In two of the fatal cases extensive pre-existing pulmonary chronic tuberculosis was detected at necropsy, in one case, general syphilitic arteriosclerosis and mild carditis were revealed, and in one case tonsillectomy had been performed two days before the onset of the pneumonia and three days prior to death.

The following table gives the death-rate obtained in cases grouped according to the type of pneumococcus as determined by the sputum.

#### MORTALITY RATE IN THE SO-CALLED GROUPS

	Group			Not		Total
	I	II	III	IV	Typed	Series
Cases .. . . . . .	43	56	13	199	11	332
Deaths .. . . . . .	4	8	0	13	0	25
Mortality, per cent....	9.3	14.2	0	6.5	0	7.7

In conclusion McClellan states that the low mortality in this extensive series of cases, together with the favorable modification of clinical symptoms by the serum, as stated above, would seem to advocate the extension of its use in pneumococcus lobar pneumonia.

In comparison with this treatment with what is put forward as a specific serum, it is of interest to note the

statistics of a series of pneumonia patients who received only the generally accepted drug treatment. Lt.-Col. Joseph L. Miller, chief of medical service and later C. O. of the Base Hospital of Camp Dodge, states that at Camp Dodge from Oct. 1, 1917, to March 20, 1918, the later date being the time when the streptococcus epidemic began, there were admitted to the Base Hospital 276 pneumonia patients of the lobar type. Only a part of these were typed, and for this reason all were classed as pneumococcus pneumonia. Thirty-one died—a mortality rate of 11.2 per cent. Fifteen of the deaths were due to empyema and in eight of these the hemolytic streptococcus was present. If these eight deaths are deducted it leaves a mortality of twenty-three or 8.3 per cent.—B.]

**Bronchopneumonia Following Measles.** This article is based on observations made by S. F. Braud,<sup>1</sup> while stationed in military service.

Between Dec. 1, 1917, and March 1, 1918, 716 cases of measles came under the author's observation, and these presented the following complications:

	Per Cent.
Otitis media, acute, suppurative.....150	20.0
Bronchopneumonia ..... 89	12.5
Septic arthritis, non-suppurative..... 12	1.5
Septic arthritis, suppurative..... 1	0.1
Meningitis, streptococcus ..... 2	0.25
General sepsis ..... 3	0.4

Of the bronchopneumonia patients, forty-two died, giving a mortality of 47 per cent. Of the total number of measles patients, forty-four died, giving a percentage of 6.1 per cent. In every case of pneumonia, *Streptococcus hemolyticus* was isolated either in the sputum or lung tissues. Eighty per cent. of the pneumonia patients developed empyema.

The following treatment was ordered in all the cases:

Tincture of digitalis, minims 15 for a period of seventy-two hours, given every four hours.

Liquids, lemonade, orangeade, grape juice and milk and water *ad libitum*.

Sodium citrate, grains 15, every three hours.

Low cleansing enema daily if no bowel movement.

(1) New Orleans Med. and Surg. Jour., June, 1919.

Temperature, 104° F. or above, give tepid sponge bath.

For insomnia, restlessness or severe cough,  $1\frac{1}{4}$  grain morphine sulphate with  $1\frac{1}{150}$  grain of atropine sulphate.

If in this scheme of treatment the digitalis did not produce the desired effect in seventy-two hours, the dose of tincture was increased from 15 to 25 minims. In a group of twenty patients, the author did not use digitalis, but gave instead caffeine citrate in 3-grain doses every four hours. The results obtained in this way were not so good as those obtained with the use of digitalis.

Ten patients were given antistreptococcus serum. After a careful desensitization of the patients 50 c.c. of the serum with 50 c.c. of normal saline solution were administered. This was repeated in from eighteen to twenty-four hours. This group was entirely too small from which to draw any conclusions, but it is the author's belief that some patients were materially benefited by the serum.

In the beginning of the epidemic, it was customary to drain from the chest all fluids which contained either the pneumococcus or the streptococcus. This procedure met with failure. Later in the epidemic the chests were aspirated every two or three days until the general condition improved. Pus formed in almost all the cases in from one to three weeks. The end-results by the second scheme were a good deal more gratifying than by the first.

## MENINGITIS AND MENINGOCOCCUS INFECTIONS

**Clinical Picture.** In one of the Lumleian lectures, Sir Humphrey Rolleston<sup>2</sup> deals with the clinical pictures of cerebrospinal fever. He discusses at some length the incubation period, the onset, and the various clinical forms. Under this last heading he mentions first, fulminating cases, which are fatal within forty-eight hours or less of the onset, are extremely dramatic from their rapid course, are of medicolegal interest and the subjects of

---

(2) Lancet, April 12, 1919.

inquests. The ordinary acute form is mentioned next. In this, the onset is sudden, and after a short interval meningitic symptoms appear, stiffness and contraction of the neck, very violent headache, Kernig's sign, and a state of cerebral irritation supervenes passing, if unrelieved by treatment, into coma.

The abortive forms are those in which the infection does not extend beyond the blood stream, and in these patients the symptoms rapidly subside after from two to six days.

Chronic forms are found in patients who are not treated at all or, if so, insufficiently; patients with meningococcus septicemia which may precede, follow, or occur without meningeal infection; patients with meningitic adhesions and obstruction to the free circulation of the cerebrospinal fluid, so that parts of the cerebrospinal subarachnoid space or the cerebral ventricles become cut off and form closed cavities inaccessible to serum injected intrathecally in the ordinary way.

There follows some discussion of encysted loculated meningitis, closed ventricular meningitis, ventriculitis, ependymitis, and hydrocephalus.

The importance of making bacteriologic examinations for a correct diagnosis of the disease is next emphasized. This examination must apply both to the cerebrospinal fluid and the blood. In making the diagnosis, cerebrospinal fever may be ruled out by failure of bacteriologic methods to give positive results, but this error is probably much less than that which would result from the inclusion of cases diagnosed on clinical grounds, and in the latter event it would be difficult to decide where to draw the line.

No specific clinical manifestation is pathognomonic of meningococcus infections. In the presence of an epidemic, an acute onset with fever, vomiting, severe headache and malaise may well arouse suspicion, but a similar train of symptoms may occur in many toxic conditions and accompany acute infections such as influenza, pneumonia, enteric fever, otitis and malaria.

The hemorrhagic rash, although highly suggestive of meningococcemia may be present in pneumococcus, streptococcus, influenza infections, and in malignant forms of



exanthemata such as smallpox. From other forms of meningitis, such as tuberculous, pneumococcus, otitic, and influenzal, an undoubted diagnosis can be made only by lumbar puncture and examination of the cerebrospinal fluid. Each of these points is discussed at some length under the heading of differential diagnosis of the disease. Diseases which produce meningism, and which may be confused on this account with meningitis, are listed as pneumonia, otitis media, acute malaria, tonsillitis with enlarged cervical glands, rheumatic stiffness of the neck, measles and rubella, rheumatic fever and spiriochetosis icterohemorrhagica. Resembling meningitis are acute infective polyneuritis, anthrax infections with cerebral symptoms, meningeal hemorrhage from various causes, as the meningitic form of acute poliomyelitis.

Encephalitis lethargica was first thought to be meningococcus meningitis, but lumbar puncture puts this diagnosis out of court. The cerebrospinal fluid in this disease is clear and the cell content usually normal; if there be any cytologic change it is in the direction of lymphocytosis. Another difference from meningococcus infection is the absence of a hemic leukocytosis. The striking features of the disease are lethargy, and ocular paralysis, though the latter is not constant, and these should arouse suspicion. On the other hand, the patient may have erythematous or petechial rashes, herpes, swelling of the joints and vomiting. When first seen some cases of meningococcus meningitis may suggest ordinary epilepsy, deafness, or even strychnine poisoning; this is especially likely to occur in sporadic cases or at the commencement of an outbreak. Other conditions that must be differentiated from meningitis are uremia, purpura hemorrhagica smallpox, malignant measles, typhus, severe food poisoning, and osteomyelitis of the spine.

#### **Determination of Type of Meningococcus Infection.**

At present the method of determining the type of meningococcus infection is to isolate the organism, and then to perform the agglutination or absorption test. This requires two or more days. As the early administration of serum in cerebrospinal meningitis is just as necessary as in pneumonia, a rapid method of determining the type of this infection is of great value. A precipitin test has

given very encouraging results. The method is described as follows by G. H. Robinson<sup>3</sup>, of Baltimore.

The spinal fluid from the patient is centrifuged until clear; 0.5 c.c. of this fluid is added to an equal amount of each of the four type sera; the tubes are thoroughly shaken and warmed to 37° C. in a water bath. If a positive reaction is obtained a distinct flocculent precipitate forms in a few minutes.

The author has not been able to obtain fluid from patients known to be in the early stages of the disease. The fluids tested were from patients who had been ill from one to two weeks. Treatment from type serum could not be obtained in all cases. In two instances in which type sera were used a prompt and distinct improvement followed.

**Extrameningeal Meningococcus Infections.** The meningeal picture resulting from meningococcus infection has so fixed the attention of clinicians and pathologists that the possibilities of extrameningeal infection by the organism has had scant notice. This has resulted in a general failure to recognize the fundamental nature of the disease as a meningococcus septicemia, which has in turn had important consequences in the fields of diagnosis and treatment.

These statements are made by W. W. Herrick,<sup>4</sup> Major, Medical Corps, U. S. Army, who reports the study of extrameningeal meningococcus infections observed at Camp Jackson, South Carolina.

Three hundred and fifteen patients who suffered from meningococcus infections were studied at that place. In approximately 40 per cent. of these the diagnosis was made before meningitis developed. In 5 per cent. meningitis never developed at all. With few exceptions the earliest evidences of meningitis were preceded by symptoms of a general infection lasting from a few hours to several days, in exceptional instances, weeks. This initial stage of sepsis was repeatedly proved by blood culture, by clinical studies and necropsy. It is not the author's opinion, however, that epidemic cerebrospinal meningitis is a sepsis throughout its entire course. He considers it

(3) New York Med. Jour., March 15, 1919.

(4) Archiv. Int. Med., April, 1919.

a blood-stream invasion, a sepsis at first, for a period averaging forty-eight hours, often more, at times less. Later, there is the local process, usually in the meninges, not infrequently elsewhere.

Emphasis on these points is considered imperative because on it is based the modified therapy, which in proper hands has mitigated the severity of the disease and greatly reduced the mortality. This treatment consists of the intravenous injection of antimeningococcus serum.

There follows a detailed record of six patients who suffered with meningococcus infections, and were observed by the author. These serve to illustrate the contention made by him, namely, that meningococcus infections frequently do not produce meningitis, and if so, at a late stage of the disease. The record of the first patient considered shows that he suffered with a meningococcus sepsis and did not have meningitis, either clinically or at autopsy. In a second instance, there was no clinical evidence of meningitis, and at autopsy meningeal congestion and arachnoid cell hyperplasia were found and were interpreted as indicating the earliest stages of meningitis.

In a third instance, there was septic polyarthrititis, the organism present being the meningococcus and this patient recovered with intravenous treatment.

A fourth patient suffered with meningitis infection for several weeks and finally developed meningitis proper.

In a fifth patient there was meningococcus, pleurisy, and in a sixth, meningococcus infection of the accessory nasal sinuses, both without meningitis.

In the opinion of the author, the term "epidemic cerebrospinal meningitis" should be abandoned, the term "meningococcus infection" should be used to denote such general processes as meningococcus sepsis. Meningococcus meningitis should be the term used in meningococcus infections with predominant cerebrospinal symptoms.

**A Clinical Study of Meningitis at an Army Camp.** This report is based on studies made during an epidemic of meningitis at Fort Riley, Kansas, beginning Sept. 23, 1917, and extending over a period of ten months, during

which time 215 patients were afflicted with the disease. The report is made by Majors W. J. Stone and R. C. P. Truitt,<sup>5</sup> of the U. S. Army, and is presented as a review of the important diagnostic features from which certain conclusions of interest and importance are drawn.

During the period in which this epidemic occurred, the incidence of meningococcus meningitis to all hospital admissions was 0.77 per cent.; 89 per cent. of the patients who developed meningitis were found to be from the rural districts. Of the 215 patients studied, 191 had meningococcus meningitis and the mortality in this group was 28.8 per cent.

There were twenty-four instances of meningitis due to other infections than meningococcus, and thirteen of these were found to be mixed infections. The mortality in this group of thirteen was 92.3 per cent. In the group of eleven patients without mixed infection, but who had meningitis due to some organism other than meningococcus, the mortality was 81.8 per cent.

Of the patients, 92 per cent. were white, 8 per cent. colored. Among the white patients who had meningococcus meningitis the mortality was 29.7 per cent. Among the colored patients the mortality was 18.7 per cent. The same difference in mortality was noticed in meningitis of all types of infection.

In making a study of the epidemiology at this camp, the carrier problem was attacked by making cultures from the nose and throat in all soldiers who had been in contact with cases that developed meningitis. The first 2,557 cultures from contacts revealed 2.5 per cent. carriers.

During the period of nine months, over 195,900 cultures were taken. At the height of the epidemic the percentage of positive cultures was over 5 per cent. but for the entire series approximately 2 per cent. showed positive cultures of meningococci. It is noted that the percentage of carriers showed little variation during the months of October, November, December and January, and yet there were about three and a half times the number of admissions for meningitis in November as in January. Such facts, while admitting various interpre-

(5) Archiv. Int. Med., March, 1919.

tations, leave open to serious doubt, the authors consider, certain established theories that the carrier markedly influences, except in a sporadic manner and in susceptible individuals, the spread of epidemic meningitis. They advocate that each person who is definitely established by cultural methods as being a chronic carrier should be isolated and kept in the open air as much as possible, and receive treatment in the way of mild nasal sprays and gargles. A 2 per cent. solution of silver nucleinate or a nasal spray of warm physiologic sodium chloride solution and a gargle of liquor sodii boratis compositus (N. F.), to which has been added one drop of phenol to the ounce, is recommended as appropriate treatment for isolated carriers. A week of such treatment is recommended. It is believed that a carrier is not necessarily a menace to other individuals unless it can be proved that he harbors virulent organisms. Two methods of transmission of the disease may occur. Avirulent organisms are transmitted to an individual who is specifically susceptible, and this person may or may not develop the disease. On the other hand, virulent organisms are transmitted to an individual with specific susceptibility.

In considering immunity in meningitis, the authors point out that of 191 patients with meningococcus meningitis ten gave a history of an earlier carrier state. Of these, two died. Nasopharyngeal cultures taken from patients suffering with the disease gave positive results in 10 per cent. of those patients examined. Two patients suffered second attacks of meningococcus meningitis within four months of the onset of their first attack. One of these patients became sensitized to serum on treatment of the first attack and was therefore given in his second attack sensitized vaccine in doses of from 500 to 2,000 millions every alternate or third day, with marked improvement in his condition. About twelve injections of vaccines were given altogether and he recovered from his second attack also.

In describing the symptoms observed, it is said that in most cases such onset of headaches, stiff neck, nausea or vomiting, chills, followed in a few hours by delirium and coma constituted the most frequent clinical picture observed. This set of symptoms developed and resulted in



delirium and coma very rapidly in many instances, so that it was not infrequent to find patients in coma in bed in the morning who had retired feeling fairly well the night before. Kernig's sign was positive in 67 per cent. of the 156 patients who recovered. A leukocytosis varying from 15,000 to 35,000 was an important early symptom.

Abortive types of meningitis were not infrequent among soldiers in the camp where this epidemic occurred. Many presented symptoms of the disease, but in the spinal fluid meningococci could not be found, and the cultures of the blood were also sterile. In such abortive types with marked clinical evidence of the disease, especially in the presence of an epidemic, the authors say that serum should be administered after free drainage at the time of diagnostic puncture. The recognition of such abortive types is difficult because of the possibility of meningismus associated with a beginning pneumonia, the presence of acute cerebrospinal syphilis, of early tuberculous meningitis, of catalepsy or of hysterical states associated with fever.

In discussing complications they state that the serum rash and arthritis which occurred in about 30 per cent. of the patients who recovered were of transitory duration as a rule. In only one instance did culture from aspirated joints show meningococci. Temporary deafness occurred in about 7 per cent. of the recovered patients. Permanent nerve deafness, bilateral, occurred in 3.6 per cent. Mixed infection was the most serious complication as to prognosis.

Discussion of the pathology of this condition is based on the records of twenty-six necropsies that were done on patients who died during the epidemic. The brain was found to be irregularly covered with a fibrinopurulent exudate that was most marked along the course of the larger blood-vessels of the cortex, about the points of exit of the cranial nerves, and at the base over the pons and medulla. There was usually a marked edema of the brain. In some instances the entire spinal cord was enveloped with exudate. Hypostatic pneumonia was frequently found to be present in patients who had been ill a number of weeks. Cultures from the brain and cord

in nearly every instance revealed meningococci while cultures from the spleen, heart blood, liver and kidneys were negative. In septic meningitis due to streptococci or pneumococci, middle-ear disease, frequently bilateral, acute mastoiditis, ethmoiditis, or empyema of the sinuses was frequently found.

Treatment of the condition was carried out by performing lumbar puncture for diagnostic purposes as early as possible on all suspects. If the fluid was under considerable pressure drainage was allowed to proceed until the pressure approximated the normal—one drop every three or four seconds. If the fluid was cloudy, an injection of 30 c.c. of serum was given without waiting for the laboratory report. The fluid in streptococcus or mixed-infection meningitis as a rule had a straw-yellow tinge, while the fluid of meningococcus meningitis had a grayish-white opaque appearance. A daily specimen of fluid was sent to the laboratory from each patient. In 90 per cent. of 215 instances the spinal fluid was distinctly cloudy on first puncture.

The usual amount of serum given intraspinally was from 30 to 35 c.c. twice daily during the first five or six days until the reports received from the laboratory showed two or more negative examinations. As a rule, the quantity of fluid drained exceeded by from 15 to 25 c.c. the quantity of serum to be given. The average amount of fluid drained was approximately 50 c.c., but in a number of instances quantities varying from 70 to 85 c.c. were obtained without markedly decreasing the pressure, in which case larger quantities were secured. The average number of intraspinal treatments in 136 recovered patients was eleven; the average total amount of serum received by each was 305 c.c.; the average total drainage of spinal fluid was 571 c.c. The average stay in the meningitis section among these recovered patients was fifty-two days.

Reference is made to the work of Herrick and Netter who used extensively the combined intravenous and intraspinal therapy in meningitis. In the work at Fort Riley only 6 per cent. of the recovered patients showed petechiae. Among the fatal instances, 14 per cent. showed this symptom. Included among these were the

rapidly fulminating types with death in a few hours. In some of these, the cerebrospinal evidences of the disease were found to be slight on necropsy, although the meningococcus was obtained by culture. Combined intravenous and intraspinal therapy was used on thirty-two patients in this work.

The authors feel that patients manifesting petechiae as evidence of blood-stream invasion should receive intravenous injections of serum in doses of 60 to 100 c.c. daily during the first three or four days of the disease, as well as intraspinal injections varying from 30 to 40 c.c. of serum twice daily. If success is to be secured, early energetic treatment is essential and is of greatest value during the first three or four days. During the course of treatment in a number of instances in this work, the spinal fluid became decreased in quantity, which made it exceedingly difficult to administer intraspinally a sufficient amount of serum without danger of increased pressure. In such cases, it was assumed that ventricular or canal blockage had occurred. In a patient who still manifests evidences of the disease, such as positive organisms, or fever, in whom mechanically it becomes difficult to continue treatment by spine, the attempt should be made to give serum by the veins. In a fairly large percentage of such cases serum reactions will occur, but the authors believe that the danger of such reactions especially if atropine or epinephrine be used and if desensitization has been properly carried out, is infinitely less than the danger of stopping all serum treatment. Those patients who developed herpes labialis were treated by alkalinizing with soda bicarbonate. The authors emphasize particularly the fact that early intensive treatment is necessary to secure results, and they strongly feel that harm may be done by over-treatment after the first ten days or two weeks.

Regarding prognosis they say that if the disease can be recognized early, and if it can be efficiently treated, the mortality should not be greater than 20 per cent., which would be in marked contrast to statistics covering the period before the adoption of a potent antiserum. The future promises still greater reduction as experience and judgment in its use accumulates, especially in the

use of convalescent human serum for the treatment of the acute disease, a plan for which has been worked out in the hospital.

**A Ward Epidemic of Meningococcus Meningitis.** During the epidemic in the autumn of 1918, one of the medical wards at Camp Jackson, Columbia, S. C., was converted into a pneumonia ward in charge of G. R. Wilkinson.<sup>6</sup> About ten days after this change was made, a case of meningococcus meningitis developed, followed by three the next day and two on the day following. Six cases developed here within a period of fifty hours. About two weeks later, two more cases developed within forty-five hours of each other in this ward. A search for the source of the infection disclosed the fact that none of the unfortunates had to their knowledge been exposed by contact to any meningitis prior to their admission to the ward. Throat cultures were immediately made of all the ward attendants, and patients, three cultures each for the attendants, and two each for the patients. It was learned that one of the newly assigned corps men in the ward had himself been a victim of the disease during the preceding winter, and worked as an attendant in the meningitis ward for some time afterward. The only positive culture found from all those taken in looking for carriers was that from the corps man mentioned here. The carrier suspect was immediately transferred to the meningitis ward, where treatment was instituted to rid his nasopharynx of the organism. Further attempts to find a positive culture in his person were unsuccessful.

A slight amount of information as to the period of incubation of the disease is shown by the fact that each group of cases developed within a period of fifty hours of each other. The first group coming on from seven to thirteen days after exposure to the carrier, and the second group developing the disease in from eighteen to twenty-one days after exposure to the carrier, or from nine to fourteen days after exposure to the other patients.

This would indicate that the incubation period is

---

(6) Jour. Amer. Med. Ass'n, June 21, 1919.

between one and two weeks. It is important to note that the disease in the two patients in the latter group ran a much milder course than those in the first group. This probably means that these persons contracted the disease from the first group of patients, thus lending weight to the doctrine of attenuated virulence by passage through another individual.

**An Epidemic of Meningococcus Meningitis Among a Chinese Civil Population.** During the spring and summer of 1918, a study was made of an epidemic of meningococcus meningitis occurring among a civil population in a district in South China. The author, P. K. Olitsky,<sup>7</sup> New York, states that an epidemic of meningococcus meningitis heretofore among the Southern Chinese is practically unknown, hence, when the first cases occurred, proper diagnosis of the patients was not made.

While there were official records for only 1,041 patients who suffered with this disease, it is estimated that at least 2,500 were affected. Among the cases reported the mortality was 85 per cent. Olitsky points out that this epidemic occurred in the subtropical zone bordering on the tropical zone, and the question is raised as to whether or not this disease is one of the temperate zone only.

The observations upon which this paper is based were made at a local hospital where none but Chinese were received. Four hundred and seventeen patients were studied in this hospital, but it is noted that modern medicine is not favorably entertained in every part of China, therefore, modern treatment could not be administered in all instances.

One hundred and four patients received neither serum treatment nor lumbar puncture; of these, 84.6 per cent. died. In 346 patients lumbar puncture was made from one to five times; of these 54.1 per cent. died. In seventy-one patients lumbar puncture combined with spinal injection of antimeningococcus serum having a low antibody content was made; of these 45 per cent. died. These sera were on hand before the author's arrival.

Conclusions to be drawn from these statements are,



first, that the mortality in this disease is appalling when no treatment is given. Second, spinal tapping by itself, while showing an improvement in the death-rate is still far from a satisfactory therapeutic procedure. Third, the injection of a serum poor in quality offers slightly better hope. And, therefore, a serum low in agglutinin content is apt to be therapeutically ineffective.

When these methods of treatment are compared with results recently obtained in civil and military practice by proper antimeningococcus serotherapy, it is certain that the employment of the latter is indicated at all times.

Blood culture studies in this work consisted of making cultures of the blood of ten patients, four of which yielded positive blood cultures; but of these four all died one day after the culture was made. The evidence is too scant to indicate whether the infection was primary or secondary in the blood in these instances. However, the results serve to emphasize the desirability of intravenous therapy.

Spinal cultures in a pure state were obtained in about sixty of these patients. Fifty-nine of them were examined at the height of the epidemic. Of these, fifty-six yielded para types and three yielded irregular para types. It is concluded, therefore, that during the height of the epidemic almost 95 per cent. of the patients were infected by the same type of meningococcus, the para type.

Attention is called to the fact that two of the cultures isolated three years previously in the Philippine epidemic were tested and found to be para type.

In a bacteriologic study made on carriers, seventy-one Europeans were examined, and of these seven were carriers, 9.8 per cent.; 133 Chinese were examined and nine found to be carriers, 6.7 per cent. From this it may be concluded that carriers were more prevalent among the white population notwithstanding the fact that very few of the latter were afflicted, 4 to 2,500 of the Chinese.

In order to study non-contact carriers, the inmates of a local jail in which no case of epidemic meningitis developed throughout this epidemic were taken as a suitable source for the determination of the number of car-

riers for comparative study. The total number of Chinese prisoners examined was 151; 24.6 per cent. of these were found to be carriers of organisms indistinguishable from meningococci. These carriers yielded types which generally were not found among the patients, namely, normal, irregular or inagglutinable organisms. Also, the percentage of carriers in the jail was higher than that demonstrated by others among the contacts with patients during the epidemic. Among these 600 or more prisoners it is noted again that no case of epidemic meningitis developed.

Among other epidemiologic factors considered is that of age. The ages of the patients ranged from 4 months to 59 years; the average age was 22.68 years. The greatest number of cases occurred between the age of infancy and 5 years. A smaller number was found at 17½ years. There was no appreciable differences in the sexes except among the young adults, where the number of male patients predominated.

In considering the influence of meteorologic conditions it was noted that when there occurred a sudden drop of temperature, the number of cases increased and when there was a rise in temperature the incidence of epidemic meningitis declined. It was also noted that the increase in cases during certain periods was in inverse ratio to the amount of sunshine present during that time.

There is further discussion of the habits of the Chinese, their modes of living and of various factors that had to do with the epidemic. Most important among these, no doubt, was the fact that dense overcrowding of population and the pathogenic type of meningococcus, rather than the actual numbers of healthy carriers of various types of the organisms, were the causes of the great spread of this epidemic.

**Pneumococcus Meningitis.** The treatment of pneumococcus meningitis by a specific antipneumococcus serum is recorded by Lawrence Litchfield.\*

The work was carried out at Camp Grant, where during a period of eight weeks, the author and his coworkers observed over 10,000 cases of influenza, with about 2,700 cases of pneumonia.

(CS) Jour. Amer. Med. Ass'n, May 10, 1919

The medical officers were asked to report at once any cases showing signs of meningeal irritation. Nearly a month after the onset of the epidemic, cases of pneumococcus meningitis began to appear.

The opportunity of treating ten patients with typical pneumococcus meningitis with the Kyes serum was presented. The clinical diagnosis in all of these patients was verified by consultants, and the etiology was established in each case by abundant laboratory findings.

Of the ten patients five died and five recovered. So far as the meningitis was concerned, there was no difference clinically between the condition of the patients who recovered and the condition of those who died. Some of the patients with the most intense symptoms of meningitis recovered. Some of the milder cases ended fatally owing to extensive involvement of other organs, as was shown by necropsy. The treatment was the same in all instances.

The dose of serum given intraspinally was usually 10 c.c., although as much as 20 c.c. of the antipneumococcus serum was injected intraspinally twice daily for as long as six days at a period. During the same time, 5 c.c. were also given intravenously twice daily.

A detailed record of each of the five patients who recovered by this treatment is presented.

**Variation of Strength in Antimeningococcus Serum from Different Sources.** Experiences with epidemic meningitis, as encountered with the American forces in Coblenz, Germany, are recorded by J. F. Robison and J. R. Gestley.<sup>9</sup>

In treating ten patients at Coblenz with an American antimeningococcus serum, no favorable results were obtained; nine of the ten died. Immediately after this, forty-five patients were treated with serum obtained from the Pasteur Institute in France and none of these died. It was found that the serum that failed in the first ten instances did not agglutinate organisms from those patients, and that the serum used in the forty-five patients following did agglutinate the organisms obtained from these patients.

From these observations, the authors conclude that

---

<sup>9</sup>9. *Jour. Amer. Med. Ass'n*, Oct. 11, 1919.

bacteria may vary according to geographic locations. Perhaps the first serum failed because in its manufacture strains of organisms indigenous to Germany and France were not included. This at any rate is a theoretical possibility. The conclusion of vital clinical importance is that if a patient with epidemic meningitis does not respond at once to intraspinal treatment, one should not temporize. The agglutinating property of the serum against the patient's own organism should be tested, and if the laboratory evidence is unfavorable, more satisfactory serum should be procured at once.

### **Statistics of Meningococcus Meningitis at Camp Lee.**

The statistics obtained in the treatment of meningococcus meningitis at Camp Lee are presented with considerable discussion of the same by R. I. Haden,<sup>1</sup> Lieutenant M. C. U. S. Army.

Reference is made to the work done on patients with meningococcus meningitis at various other camps, and detailed records of a few patients are presented. The author's experience, which is the basis of this paper, consisted of treating twenty-one patients who had meningococcus meningitis at Camp Lee during 1918; twenty-one, or 67.7 per cent. of these patients presented unmistakable evidence of a generalized infection before there was a localization in the meninges.

The mortality of the entire series was 22.6 per cent.

During the period of intraspinal treatment alone, and combined intraspinal and intrasubcutaneous treatment the mortality was 37.5 per cent.; during the period in which intraspinal and intravenous therapy was employed the mortality was 6.6 per cent.

It is concluded that meningococcus meningitis, in probably every case, is primarily a generalized infection with subsequent meningeal localization.

The use of immune serum intravenously marks a great advance in the treatment of the disease.

Prolonged intraspinal treatment is very apt to result in permanent ill effects from the involvement of the cauda equina and nerve roots.

Intravenous treatment decreases the number of intra-

---

(1) *Archiv. Int. Med.*, November, 1919.

spinal treatments necessary, thus minimizing the harmful effects of local treatment.

One case is reported in which an active localized infection in the meninges recovered under intravenous therapy alone.

**Acute Streptococcus Meningitis with Recovery.** A single case of streptococcus meningitis with recovery is recorded by G. H. Weaver,<sup>2</sup> because instances of recovery from streptococcus meningitis are uncommon, and the case presents some other points of interest.

The patient was a woman, 25 years old, who became suddenly and violently ill with headache, vomiting and severe pain in the back of the neck and the back. At midnight of this day, a lumbar puncture was made which yielded a turbid fluid, containing abundant polymorphonuclear leukocytes. No bacteria were with certainty found in smears. Twenty-seven cubic centimeters of antimeningococcus serum were given intraspinally.

On the following day, lumbar puncture yielded 25 c.c. of turbid fluid after increased pressure which contained 2,759 cells per c. mm., most of them being polymorphonuclear leukocytes. No bacteria were recognized in smears and 20 c.c. of antimeningococcus serum were given intraspinally. Culture of the spinal fluid on blood-agar plates gave a pure growth of small white colonies of a Gram-positive streptococcus in moderate numbers. This organism was identified as *Streptococcus viridans*.

From September 23 to October 18 frequent spinal punctures were made and polyvalent antistreptococcus serum was given intraspinally. Improvement that followed each administration of the serum was striking. On October 21, 25 c.c. of the serum were given intravenously, and improvement was greater from that day on than had been noted before.

In cases of streptococcus meningitis which are usually hopeless, the combined intraspinal and intramuscular administration of antistreptococcus serum would seem to be worth trying. The curative action of the serum depends largely on its opsonic content, as does that of antimeningococcus serum and, theoretically, the serum

---

(2) Jour. Amer. Med. Ass'n, May 10, 1919.



should be useful in such a condition as meningitis, in which it can be brought in direct contact with the bacteria.

## POLIOMYELITIS

**Persistence of the Virus of Poliomyelitis in the Nasopharynx.** This paper by S. Flexner and H. M. Amoss<sup>3</sup> is presented as a contribution to the epidemiology of poliomyelitis. They state that present knowledge places that disease among the infections in which the specific cause is carried in the nasopharynx, and that present belief is to the effect that the virus is conveyed from one person to another through the medium of the nasopharyngeal secretions. Indeed, the virus has been detected in these secretions by the inoculation tests in three sets of conditions: coincidentally with an attack of the disease incited by it; a considerable period after the attack of acute disease has abated; and in healthy persons who have been in contact with cases of poliomyelitis.

After reviewing the literature on this subject, a brief description of experiments carried out by the authors is given. These experiments were made with human materials of two sorts: namely, tonsils and adenoids removed during life, and tonsils and pharyngeal mucosa excised after death. The object in all the experiments was to ascertain the presence of the virus so far as this could be determined by the inoculation test. In this way, it was hoped to throw light on the persistence of the virus in nasal and buccal membranes and their discharges.

The results obtained by this work conform closely with clinical experience in the United States, at least, and especially with the observations made by epidemiologists in the course of the wide epidemic in New York State and elsewhere during the summer and autumn of 1916. The conclusion reached at the time was to the effect that the communicability of the disease was a phenomenon chiefly of the early stages, while the frankly paralyzed person and the convalescent were to be feared much less.

In the experiments, infection was secured with tissues

(3) Jour. Eper. Med., April, 1919.

obtained during the first week, approximately, of the disease but not at the later periods.

The authors conclude that the virus of poliomyelitis occurs in the nasopharynx of man and monkeys.

In man it has been detected by the inoculation test in washings from acute cases, rarely in similar washings from healthy contacts, in the nasopharyngeal tissues obtained from fatal cases in the first week of infection but rarely, if ever, from nasopharyngeal tissues removed surgically at later periods in the course of the disease.

In monkeys, also, the virus has been detected in the secretions from acute experimental infections, in the nasopharyngeal tissues derived from early cases, and rarely from cases several weeks or months after recovery from the acute symptoms.

The inoculation of tonsils and adenoids from cases of undoubted poliomyelitis either yielded definite results in the form of typical paralysis and histologic lesions in the central nervous organs of the monkeys injected, or no symptoms, or lesions which could be confounded with poliomyelitis. The indefinite symptoms and atypical lesions described in a certain class of inoculated animals by Kling, Pettersson, and Wernstedt were not encountered in the present experiments.

The deduction from the experiments reported is to the effect that the virus is regularly present in the nasopharynx in cases of poliomyelitis in the first days of illness, and especially in fatal cases; that it diminishes relatively quickly as the disease progresses, except in rare instances; and that it is unusual for a carrier state to be developed. Hence the period of greatest infectivity of patients would appear to be early in the disease, which is probably the time at which communication of the virus from person to person takes place.

Available evidence proves that healthy carriers of the virus occur. Data which are not at hand indicate the frequency with which carriage arises. The fact that even after a severe and wide epidemic, such as occurred in the United States in 1916, the disease may virtually disappear within two or three years points to the probability that enduring carriers of the active virus, whether healthy or chronic, are of exceptional occurrence.

## RHEUMATISM AND ARTHRITIS

**Rheumatism in the Light of Modern Research.** During the past ten years, physicians have learned that conditions which were previously regarded as rheumatic may now be divided into two classes, about 70 per cent. being due to various types of focal infection and about 30 per cent. to disturbances of the metabolic processes—that is, too much food in general, too much of one kind of food, such as potatoes, rice, meats, oranges, etc., some physiologic disturbance of the function of digestion to digest certain kinds of food.

H. W. Frauenthal<sup>4</sup> calls attention to the fact that there is no form of septic or infective disease affecting the body which may not produce acute and chronic inflammation of joints. For instance: 1. Any local nidus of suppuration in the oral or nasal cavities, as carious teeth, septic gums or tonsils, rhinitis, and accessory sinus disease, middle-ear suppuration, and the like.

2. Acute or chronic infection of the genito-urinary tract—urethritis, prostatitis, vesiculitis, cystitis, and nephritis, vulvovaginitis, endometritis, pyosalpinx, etc.

3. Puerperal sepsis.

4. All forms of gastro-intestinal disease, from gastritis or the mildest mucous colitis or a peri-anal abscess, to the gravest forms of ulcerative colitis.

5. Sepsis in the bronchial and pulmonary systems, from acute bronchitis to the most chronic form of bronchiectasis.

6. Every known specific bacterium has been proved a source of arthritis—streptococcus, staphylococcus, pneumococcus, gonococcus, typhoid, *S. crysipelatis*, meningococcus, the bacillus of dysentery, *S. salivarius*, etc.

7. The exanthemata and infective diseases common to childhood, diphtheria, chickenpox, scarlet fever, and measles.

8. Acute rheumatism, which probably affords one of the best examples of acute synovitis. It is also associated with suppuration in joints, as one would expect in an affection which so frequently leads to malignant endocarditis and septicopyemia.

(4) New York Med. Jour., Dec. 20, 1919.

[When a pyogenic process develops in acute rheumatism, the infectious agents are mixed, or the original and primary invading strain of microorganisms have taken on added virulence with pyogenic qualities. Typical acute rheumatic arthritis is not suppurative.—B.]

9. The chronic granulomata, syphilis and tuberculosis.

10. Many diseases incidental to the tropics.

11. Lastly, any lesion, however small or unexpected, which may lead to septicopyemia, whether acute or chronic, has the capacity to infect a joint. One comes across such instances constantly.

The author also points out that a bacterial process may produce arthritis by septicemia or pyemia. That is, the bacteria themselves gain admission to the constituent tissues forming the joints and therein excite active disease. Or, the arthritis may be a result of the production of toxins in any local nidus of disease, that is, not in the joints. These must circulate in the blood-stream and thus tend to produce disease in all the tissues of the body.

Arthritis due to toxins of the circulating blood is ordinarily hypothetical. In serum disease and in the synovitis of diphtheria toxins may be the cause; but usually infectious arthritis is due to the toxins of bacteria, liberated in the tissues invaded by pathogenic bacteria.—B.]

If any portion of the body has its vitality sufficiently reduced by other agencies, such as over-use, trauma of a very slight nature, or exposure to colds, the toxins are enabled to excite inflammation in such an area, thus producing in a joint synovitis or arthritis. When, therefore, one attributes to cold and slight lesion the blame for synovitis or arthritis, he must remember that in all probability they were only contributory to it, and seek for septic foci in other parts of the body.

Frauenthal presents records of patients who have been in his care and who developed arthritis, first, as a result of infections around the teeth. Other instances have followed: secondary virulent throat infections, arthritis due to non-gonorrheal leukorrhea, gonorrheal joint disease, and syphilitic arthritis are discussed in this order.

Under the heading of treatment he says that in all

cases of focal infection, one must eliminate the spreading foci of the disease, but if it is in the tonsil, it is most advisable to remove it during the acute condition.

The physicians in this country, he says, are just awakening to the value of physical methods of treatment such as the following:

#### **Massage.**

Mechanical vibration with a regular stroke, which is more efficient in giving deep massage than the hand, as there is more power to the percussion.

Baking by dry heat in a temperature of from 150 to 400° F. to produce congestion and elimination.

Hydrotherapeutics consisting of general baths in which the trunk and limbs are immersed; aëration baths; brine baths; sedative pool baths; and body manipulation baths; and local baths, in which only the limbs are treated; whirlpool baths; septic wound baths; contrast baths, and hot and cold packs and douches and showers, low pressure douche; alternating or Scottish douche; and needle baths and showers.

The use of electric light treatment as a substitute for the actinic rays of the sun.

The use of the galvanic, faradic and sinusoidal and Morton wave current to stimulate local circulation and to aid in the absorption of articular and peri-articular exudates.

The use of diathermy for action on the central metabolic processes.

In addition, it is urged that one of the best and most efficient methods of attacking joint disease by electro-ionization is also greatly neglected. Ionic medication has the advantage over hypodermic injections. While the latter carries the drug into the lymph spaces, and to the muscles and nerves but not into the cells, by ionization a large quantity of drug can be applied to a given local area, and by this means a greater and more prolonged effect can be obtained. When lithium is administered in this way the elimination by the urine is extended over a longer period than when the drug is taken by mouth.

**Acute Rheumatism.** This contribution to the study of acute rheumatism by John Poynton,<sup>5</sup> of London, has

(5) Brit. Med. Jour., March 29, 1919.



to do with the report of a girl, aged 17, a machinist, who consulted a physician first because she suffered from weakness, nervousness, palpitation and dyspnea on exertion. She was found to be a pale, thin, delicate girl, who was obviously the victim of Grave's disease, and organic heart disease. The latter dated from an attack of rheumatic fever two years previously, and at the same time the thyroid enlargement was noted. One and a half months after she was admitted to the hospital under Poynton's care, she developed a severe sore throat, the temperature rose, and multiple arthritis affecting the ankles, wrists and shoulders followed. There also developed an unusually copious pericardial effusion. The pericardium was tapped, and 18 ounces of serofibrinous fluid were withdrawn.

The fluid was centrifugalized and both free and in still greater numbers taken up in the leukocytes were demonstrated numerous minute diplococci.

Recovery was remarkably rapid, the temperature falling to normal four days later, after a course of irregular fever lasting five weeks, and reaching at times to 103° F. The pulse-rate which had reached to 156 a minute fell to 112.

Soon after recovery from this trouble, the girl developed influenza and later had a recurrence of the thyroid symptoms.

In the opinion of Poynton, this case presents a clear issue. The patient, a victim of acute rheumatism, with a heart injured by a previous attack, passes through a second most severe one while under observation in a hospital. A general pericarditis with copious effusion develops and the fluid withdrawn by paracentesis shows numerous minute diplococci, some in the fluid, many more carried up in numbers by the polynuclear leukocytes.

The stage of the illness is one in which the acute phase is subsiding, but death is threatened from mechanical embarrassment. This patient does not die. The effusion does not return. The temperature falls and eventually the recovery is so good that she leaves the hospital, able to walk short distances, and with a compensated mitral lesion.

Poynton states that some years ago in conjunction with Dr. Payne, he recorded the isolation of the diplococcus from the blood stream and synovial fluid during life, and they have repeatedly emphasized the rapid destruction of the diplococcus in animal tissues by leukocyte and tissue cells. Now the proof of its presence is presented in the fluid from the pericardium of a patient who is living, and a further step in the organism's life history in man is gained, and further light is thrown upon the process of recovery in rheumatic pericarditis. Clearly the cells in the exudate are busy destroying the diplococci in great numbers, and one is not surprised that cultures may not prove invariably successful, for it must always be borne in mind that if the process of their destruction is already in progress, the sudden transfer to a culture medium, which can but imperfectly represent the living human medium, may give the final death blow to the harassed micrococci.

This is reported as the first case in which the author has been fortunate enough to obtain a living pericardial exudate in man in this particular phase, and it is said to completely support the results of experimentation.

**Meningococcus Rheumatism and Arthritis.** Paul Sainton,<sup>6</sup> writing in the Paris supplement to the *Lancet*, states that meningococcus arthritis may be associated with a cerebrospinal meningitis, with septicemia apart from meningitis, or may occur aside from other infections.

The frequency with which arthritis occurs during the course of meningitis is variable. In the author's observation, it occurred in 20 per cent. The date of appearance was variable, as follows: Pre-meningitic, prior to the meningitis; juxta-meningitic, during the course of the meningitis; post-meningitic, these may be either early or delayed.

In these respective groups the author observed one, two and seven cases. The types of meningococcus-arthritis are classified clinically as follows: arthralgie, acute suppurative, subacute suppurative; hemarthrosis; and plastic with early ankylosis.

<sup>6</sup> *Lancet*, June 21, 1919.

The acute suppurative type is the most frequent form, occurring in two-thirds of the patients. The articular metastasis is marked by rise of temperature, accompanied often, but not always, by labial or facial herpes, by difficulty of movement, and by hypersensitiveness of the joints, rather than by actual pain.

Suppurative meningococcus arthritis is distinguished by the following clinical features: It is indolent, or at any rate, only slightly painful. The patient does not complain of it. Even if it is not marked, it may not attract the attention of the physician. It is discovered only by a minute examination of each joint in succession. When a joint affected with meningococcus arthritis is aspirated, a liquid with special characters is obtained: it is viscous, uniform, pale grass-green in tint, and almost fluorescent in a way not found in any other form of purulent arthritis. This coloration suggests that meningococcus growing in the synovia may there find a medium favorable to the development of a chromogenic character.

The joint fluid contains abundant polynuclear leukocytes, large serous endothelial cells, occasionally free fat globules, and meningococci in abundance. Cultures from articular pus on suitable media are consistently positive; this was the case in all of the author's patients.

The course of acute meningococcus pyarthrosis is usually mild. It may end in spontaneous and rapid absorption. In the present work, joints in which pus had been found appeared to have recovered completely forty-eight hours later. Articular puncture usually leads to rapid cure.

Other types of joint lesions encountered are as follows: Subacute suppurative type, which is rare; hemarthrosis, which was not encountered at all in the present work; the plastic type with early ankylosis, of which only one instance was seen in the author's observation.

In considering arthritis associated with extrameningeal meningococcus infections, Sainton states that in a number of cases the first indication of the infection is to be found in the articular synovial membrane, giving rise to a type of acute generalized articular rheumatism. As

a rule, in the acute form the patients have a rigor, and a rise of temperature very often accompanied by herpes. The articular localizations are at least as mobile as in rheumatic arthritis, the functional disability is comparatively insignificant, and the pain is less acute than in acute articular rheumatism.

Meningococcus rheumatism rarely occurs alone; it is nearly always accompanied by other phenomena, such as cutaneous erythemia, meningococcus bronchopneumonia, orchiepididymitis and suppurative iridochorioiditis.

It is known that arthritis occurring as an isolated phenomenon and disappearing rapidly without leaving any trace may be the sole manifestation of a mild meningococcus infection; only three cases of this type, were seen by the author.

Concerning the matter of diagnosis, it is pointed out that when the articular localization of the meningococcus is super-added to a cerebrospinal meningitis, the condition is easy to recognize. This is not, however, the case when these symptoms are the initial or the only sign of the invasion of the system by the meningococcus. It is likely that during the course of an epidemic of cerebrospinal meningitis a large number of cases of meningococcus arthritis occur unrecognized. This is due to their symptomatology being inconspicuous; their characteristics of mobility, indolence, and absence of ankylosis fail to attract attention through their very modesty; they are so sketchy in their outlines that no importance is attached to them and puncture of the joint is not attempted. It is only by this procedure that they can be identified. The microscopic characters of the liquid and particularly its green tint, should arouse suspicion of the nature of the infection; this can not be verified except by finding the meningococcus in the fluid withdrawn by puncture. In cases in which the joint fluid is sterile, blood culture on appropriate media may give a clue by showing a meningococcus septicemia, or even culture from the mucus may give assistance.

Meningococcus arthritis is a sign of a more or less evident septicemia; it must be recognized that side by side with the major infections with the meningococcus

are a series of much-modified forms which are often undiagnosed.

In considering treatment, Sainton says that cure is usually spontaneous. It is remarkably assisted by the injection of antimeningococcus serum into the joint after removal of a certain quantity of fluid. On the first or second day after the injection a reaction characterized by pain and swelling is produced, but this is quick to disappear, and the effusion clears up in most cases after a single injection. The individual dose of serum given has never been greater than 10 c.cm. In one case it was necessary to perform arthrotomy: this was followed by a rapid recovery unaccompanied by any stiffness of the joint.

**Meningococcus Arthritis.** A study of an epidemic of 321 cases of meningococcus infection at Camp Jackson, N. C., from November, 1917, to April, 1919, was made by W. W. Herrick and G. M. Parkhurst.<sup>7</sup> During this epidemic, the authors were impressed with the frequency of arthritis, with the variety of its manifestations and with the clinical profit of a separation of these arthritides into different forms or types. The result of their studies has been the classification of these varieties of arthritis met with in meningococcus infection, which they present as follows:

Arthritis in meningococcus infection may appear in three forms or types, each having peculiar significance in diagnosis, prognosis and treatment. For convenience they are spoken of as "Types A," "B," and "C."

*Type A.*—As "Type A" there is designated an acute polyarthritis that is frequently the initial symptom, more often one of a number of symptoms of onset and that does not, except in rare cases, appear later than the first, second, or third day of the disease. This type is a feature of many of the cases with severe infections and is usually a harbinger of a stormy course. Almost all these cases have profuse hemorrhagic rashes coincident with the polyarthritis. In many but not in all instances the arthritis is as transitory as the rash. It would seem that these early joint symptoms are due to hemorrhage into the articular and peri-articular struc-

(7) Amer. Jour. Med. Sci., October, 1919.



tures, especially the synovia, and are identical with the hemorrhagic lesions of the skin and serous membranes.

Twelve patients were observed who had this early acute polyarthritis. Of these eight lived and four died, the mortality being 33.3 per cent.

Of these twelve patients, five had panophthalmitis, with destruction of the globe, two hydrocephalus; two epididymitis and one gangrene of the skin. Two of the twelve did not develop meningitis. Of those who recovered, five had the combined intraspinal and intravenous serum treatment, two had intraspinal and one intravenous treatment only. In the four fatal cases, two patients had only intraspinal serum treatment, one had combined intraspinal and intravenous, and one intravenous treatment alone. Patients receiving only intravenous treatment were those in whom meningitis was absent.

*Type B.*—The second type observed, designated as Type B, is differentiated from the preceding type sharply. Its onset is late, usually about the fifth day. With few exceptions only one joint is affected, generally, the knee, occasionally the ankle, shoulder, wrist or elbow. In contrast to Type A, effusion is a prominent feature, so that aspiration of the synovial capsule is suggested in many instances. Swelling is great, but redness, pain, tenderness and limitation of motion are surprisingly slight. The exudate is usually viscid, mucinous, semipurulent, not infrequently hemorrhagic. Rarely there is a thick greenish pus. Meningococci are found in at least one-third of the cases. The duration of the process is usually from one to four weeks, recovery being gradual but complete.

The prognosis in this group is good. Only 12.5 per cent. of these patients die. A total number of sixteen was observed and fourteen made complete recovery. The mortality, therefore, was 12.5 per cent. Both knees were involved seven times, both hips, both ankles, and both wrists, once each, and the right shoulder once. Of the three patients having more than one joint involved, two had both knees and one the left ankle and right wrist.

Among these sixteen cases other complications were relatively rare. Panophthalmitis occurred once, epididymitis three times, hydrocephalus twice, pneumonia and pericarditis once and gangrene once. Of those who recovered, two were treated by the intraspinal method, eight were treated by the combined intraspinal and intravenous method, and one was treated by the intravenous method alone. In the two fatal cases the patients were treated by the combined method.

*Type C.*—The third or Type C, which may be encountered in meningococcus infection, is the well-known serum arthritis. This does not differ from the serum arthritis seen after serotherapy in pneumonia or other acute diseases. In this group of 321 patients, there were twelve examples of serum arthritis, of which six were treated by each method.

In addition to these complications of meningitis reference is made to a single instance of purpura rheumatica and meningococcus sepsis. This was in a soldier who was admitted to an army hospital March 6, giving a history of an attack of tonsillitis a few weeks before, since which he had not been well. Malaise and lack of strength and energy were constant. On admission there was great soreness of the muscles and joints, a hemorrhagic eruption and a temperature of 101° F. A diagnosis of purpura rheumatica was made. Moderate polyarthritis with purpuric spots more numerous about the joints continued without meningeal symptoms until March 14, when there was note of headache and neck stiffness, which subsided. Not until March 21, was lumbar puncture done. The cerebrospinal fluid was under great pressure and contained pus and meningococci. The blood culture was negative. Combined intravenous and intraspinal treatment was given and complete recovery ensued. The facts presented by this single instance lead one to believe that the group of hemorrhagic diseases with symptoms of infection needs further bacteriologic study.

**Non-specific Hemoprotein Antigen for Treatment of Arthritis.** This communication deals with the use of protein for the treatment of acute and chronic arthritis.

and is presented by C. Brooks and F. M. Stanton,<sup>1</sup> of Columbus, Ohio.

The protein used in this work was prepared by Brooks for the purpose of combating streptococcus infection. It was a protein prepared from ox-blood fibrin by peptic and hydrochloric acid digestion, the products of this digestion being fractionated by precipitation with ammonium sulphate, the first fraction being rejected and the lower one used. The protein is prepared in a dry state and kept in hermetically sealed glass ampoules. These ampoules were sterilized by heat. When used, the dry, sterile, powdered protein was dissolved in sterile 0.9 per cent. sodium chloride solution and used at once by intravenous injection with aseptic technique. In some instances intramuscular injections were made.

The observation has been made that old rheumatic conditions have cleared up after injections of typhoid serum. Non-specific protein treatment of other diseases has been more or less successful. One disadvantage of the typhoid serum treatment is that it often brings on a rather violent reaction with rigors and high fever, depression, and other distressing and even alarming and dangerous symptoms. In the use of the protein as prepared in the way here described, no unpleasant reaction was observed at any time. At first the authors were inclined to doubt the efficacy of the protein because there was no reaction, but it seems that this depressing phase of the process is not an essential feature of antigen action. It has also been found that the preparation must be used immediately after dissolving it in salt solution, for in those instances in which there was a delay of an hour or more after dissolving the protein before the injection was made, no beneficial effects were produced, and sometimes there occurred a slight inflammatory reaction at the point of injection, when the material was used intramuscularly. This was never found to occur when the protein was injected promptly after solution. The intravenous method is considered the logical one to use. There seems to be no danger from its use. A large number of tests on animals in various doses showed no untoward results whatever. Afterward

---

(8) New York Med. Jour., March, 1919.

it was used on patients with similar results. However, many patients object to intravenous medication, but will readily agree to intramuscular injection. In such instances, the intravenous dose is doubled or tripled, and even quadrupled.

It seems that the practical results are about the same from intravenous or from intramuscular injections. However, there might be some cases which would respond favorably to the intravenous treatment, but would not to intramuscular treatment, though such cases have not been encountered by the author. The matter of dosage does not seem to be very definite, based on these experiences. Anywhere from 10 to 60 milligrams seems to do adequately well. In this work 20 or 25 milligrams were given intravenously and about 30 or 40 or more intramuscularly. The article gives detailed records of each patient who was treated in this way.

The results in all instances are rated as good, and the authors consider that they indicate a valuable remedy for this malady.

## MALARIA

**Studies on Malaria Control.** C. C. Bass,<sup>9</sup> of New Orleans, has written several articles dealing with various phases of the malaria problem: a combined abstract follows:

The first article has to do with the relative frequency of malaria in different ages and age groups in a large area of great prevalence of malaria. These observations are based on a survey made during 1916 and 1917, of all persons of all ages living in an area of 328 square miles in Boliver County, Mississippi. This is in the heart of the Mississippi delta and is one of the most intense malaria sections of the United States. A careful history as to whether attacks of malaria had occurred during the previous twelve months was obtained, and blood was collected and examined by the thick film method from 31,459 persons living in this area. All ages and classes of people were examined alike and, therefore, it is

---

(9) Southern Med. Jour., August, 1919.

believed that the results obtained are conclusive so far as that particular locality is concerned.

Of the total number of 31,459 persons, 40.30 per cent. gave a history of having had one or more attacks of malaria during the previous twelve months; and 28.96 per cent. of these were found positive by blood examination. Examinations of the blood of those who gave negative histories showed that 15.93 per cent. of them had malaria parasites in their blood. If those who gave negative histories, but who were found positive upon blood examination, are added to those who gave a definite history of attacks during the previous twelve months, an indicated prevalence of malaria during the year of at least 49.81 per cent. is obtained. This includes the entire population and shows that the observations were made in an area in which malaria is very prevalent.

It was found that the height of the infection was reached at the age of 6 and that the five-year group showing the heaviest infection was the five to nine year old group. The percentage of infection of persons under 20 years of age was 23.56 per cent. against 19.22 per cent. for persons over 20 years of age.

The population of the area studied averaged 90 per square mile, consisting of 17.8 per cent. whites and 82.2 per cent. negroes. The negroes were found to have 36.61 per cent. more infection than whites.

The distribution of the total amount of malaria in people of different ages and age groups showed that approximately 50 per cent. of all the malaria in the county occurs in persons under 20 years of age. Approximately 15 per cent. of all the malaria falls in the age group from 5 to 9 inclusive.

The second study in this group has to do with the frequency of malaria in persons without recognized symptoms, compared with the frequency of recognized attacks in an area of great prevalence.

The basis for the conclusions reached here is an analysis of the results of a malaria survey of the 31,359 persons mentioned above. These, it will be remembered, included practically every person living in an area of 328 square miles.

The facts obtained by this analysis lead to the con-



clusion that in this particular locality at least, where 40.3 per cent. of all the people give a history of having one or more recognized attacks of malaria during a year, and where at least 21.8 per cent. have malaria parasites in their blood, 55.09 per cent. of all the malaria demonstrated by blood examinations is in persons who have had recognized attacks of malaria, and that 44.91 per cent. either did not produce any symptoms whatever, or at least does not produce symptoms that are recognized as malaria. The history of the attacks alone can not be depended on to indicate the presence of malaria infection. It indicates only 55.09 per cent. of the existing infection.

Attention is called to the fact that in a group of people where malaria is as prevalent as in the locality under consideration, at least 15.93 per cent. of those who give negative histories as to the present or recently recognized symptoms of malaria have parasites in their blood. It should also be noted that because of the fact that malaria infection may be present without producing recognized symptoms of disease, finding parasites in the blood may lead to a diagnosis of malaria and to overlooking other important conditions.

In this survey, individuals found to have malaria were furnished quinine treatment. Different groups were placed on different methods of treatment, and in all of them the dose for children as compared with adults was always in the same proportion, regardless of what method of treatment was followed.

The proportion followed in the experiment was one-twentieth of the adult dose for each year of age. For instance, a child 1 year old was given one-twentieth of the adult dose used in that particular group. A child 5 years old was given five-twentieths or one-fourth of the adult dose, etc.

This fractional proportion was adhered to for all groups up to the age of 20, which was considered the adult age.

A total of 9,818 persons who had been on quinine treatment were re-examined after the treatment was completed and these examinations showed the percentage of cures obtained in the different people of different

ages. These results indicate the effectiveness of quinine in children in the proportion of one-twentieth of the adult dose for each year of age.

Since the tabulation is based on blood examinations only, the results indicate the effectiveness of the treatment in disinfecting infected persons and do not necessarily indicate the effectiveness in controlling clinical symptoms, though it is presumed that such is the case. From the results obtained it has been possible to calculate exactly what proportionate dose for each age in children would be required to produce the same effect or to disinfect the same proportion as a given adult dose does.

It is the author's opinion that 10 grains is the proper dose of quinine for adults in the treatment of malaria. This should be repeated about three times during every twenty-four hours for the first three or four days in treating acute cases, and it should then be given once each day for a period of at least eight weeks in all cases for the purpose of disinfection, and preventing relapse. The proportionate doses required for each age, to produce the same effect as the corresponding adult dose does, are indicated in the following table:

Age	Proportion of Adult Dose	When Adult Dose is 10 Gr.
Under 1	0.05	$\frac{1}{2}$ grain
1	0.1	1 grain
2	0.2	2 grains
3 and 4	0.3	3 grains
5, 6 and 7	0.4	4 grains
9, 9 and 10	0.6	6 grains
11, 12, 13 and 14	0.8	8 grains
15 or over	1.0	10 grains

The last division of this study of malaria has to do with effective immunity against malaria. A certain amount of immunity probably follows attacks of any disease from which there is spontaneous recovery or recovery not dependent entirely upon the action of a specific. Many malaria patients recover from the clinical disease and lose their infection quite independently of any specific treatment. The duration of this immunity and its effectiveness in protecting against re-infection

is uncertain. The object of this paper is to direct attention to certain observations indicating that effective and lasting immunity against malaria infection does not occur. Malaria is characterized by the production in the organs and tissues of the body of large numbers of malaria parasites and large quantities of foreign protein, the malaria parasite substance. This is set free and destroyed in the blood by the action of certain antibodies and immunity processes. Training of the tissues, as it were, to produce these antibodies and to perform these functions upon which immunity rests is to be expected.

Among the antibodies produced, in some cases, at least, the author has observed agglutination of malaria parasites cultivated *in vitro*. A lysin is also produced in malaria and is demonstrable if one employs suitable material.

Thomson is quoted as having demonstrated a complement-binding substance which seems to be present in sufficient quantities to make it possible to make the test for it a promising aid in the diagnosis of malaria. Opsonins are also probably greatly increased.

Although the antibodies and immunity processes are demonstrable, they are not sufficient to disinfect the individual rapidly, in many cases at least.

In a summary of this study, Bass states that immune bodies are produced in malaria and the immunity processes contribute largely to the elimination of the infection. In fact, they are usually sufficient to eliminate the infection in time without the aid of specific medication. In any given locality where malaria is very prevalent, if it were followed by lasting and effective immunity, there should be little malaria in older children and adults in a locality where approximately 60 per cent. have malaria during a given year. It is observed that malaria occurs about three-fourths as frequently in adults as in children. This observation indicates that whatever immunity is produced it is not lasting and effective against new infection.

**The Use of Pepsin-Quinine Mixture in the Treatment of Malaria Carriers.** This subject has been studied

by F. E. Harrington and Ethel Barrier.<sup>1</sup> During malaria investigation work in Hattiesburg, Miss., in connection with the U. S. Public Health Service, studies were undertaken in March, 1918, and continued for a period of one year, dealing with this subject. Numerous observations were made, and definite studies were undertaken to determine first, the best percentage mixture, second, the elimination of idiosyncrasies, and third, the effect of this mixture on the plasmodia in the circulating blood.

After careful investigation, the following proportion of quinine was adopted, and is here given with the results obtained, having as an object, the elimination of the unpleasant and untoward effects of quinine.

#### QUININE FORMULA ADMINISTERED

Quinine sulphate .....90 parts (by weight)

Powdered pepsin, U. S. P. .... 4 parts (by weight)

Mix thoroughly and place in capsules No. 0 or No. 3.

This mixture gave in capsule No. 0 4.97 grains of quinine sulphate. The authors conclude that the administration of quinine-pepsin mixture reduces the incidence of unpleasant results about 70 per cent., as compared with the idiosyncrasies manifested following the administration of plain quinine sulphate, without any evidences of impairing the effect on the plasmodia in the circulating blood.

**Wassermann Reaction in Malaria.** While working on a special malaria research for the British war office, it was suggested to J. Gordon Thomson and Claude H. Mills,<sup>2</sup> that it would be of great value to test a series of malaria cases by one of the standard Wassermann methods used for the diagnosis of syphilis. Following this suggestion, the authors carried out the Wassermann tests on the blood serum of 130 patients who had a positive diagnosis of malaria.

A brief review of the results obtained by other workers in this field is first presented. Judging by the results reported by twenty-one different workers, it is evident that the term "Wassermann test" has been

(1) Southern Med. Jour., August, 1919.

(2) Lancet, May 10, 1919.

employed in a very loose sense. Many writers have not even taken the precaution of describing the method used. The contradictory results and consequent confusion which have arisen since 1909 have undoubtedly been caused by different laboratory workers using a variety of methods, some of which must have been unreliable. In addition to this, it must be recognized that in many cases latent syphilis is difficult to exclude, even with the aid of a specialist accustomed to the clinical aspects of this disease.

From a summing up of the literature, the authors conclude that the cases of malaria credited with giving a positive Wassermann reaction are extremely rare. Of the patients studied in this work 122 gave a clearly negative Wassermann reaction and eight a positive reaction. Considerable information concerning each of these patients is included in an extensive table. The results are also discussed at considerable length. The conclusion reached is that the Wassermann reaction conducted according to a recognized standard method does not give a positive reaction in malaria at any stage of the disease. If a positive Wassermann reaction is obtained in a case of malaria, it is either due to undiagnosed syphilis or to faulty technique.

**Control of Malaria in Arkansas Rice Fields.** An account of methods to control effectively malaria in a rice field district, with observations on experimental mosquito bites, is recorded by J. C. Geiger and W. C. Purdy.<sup>5</sup>

This work was carried out at Lonoke, Arkansas, which is situated in the rice growing district and where mosquitoes and malaria constitute an important problem in the health of the community.

The principal methods adopted to control the disease were sterilization of carriers to prevent infection by mosquitoes, screening to prevent the access of mosquitoes to men and limitation of the production of mosquitoes so far as was found practicable.

In order to find human carriers, two separate blood indexes, thick smears, were made of every resident in

---

(5) Jour. Amer. Med. Ass'n, March 22, 1919. Another article on this subject discussing the public health standpoint is abstracted in Practical Medicine Series, 1919, Vol. VI, pp. 348-351.



the Lonoke District. The taking of blood smears and the checking up of the residents were accomplished by making card indexes of the occupants of each house, store and building. So far as possible, examinations were made of new residents also. Of the persons from whom thick blood smears were taken, ninety were found on microscopic examination to be carriers, every one of whom was treated with quinine in capsules by mouth. Each carrier was followed for thirty days so as to make certain that the treatment was actually carried out. At the end of thirty days individual patients were given quinine sufficient for a like period of time, with instructions to use as in the first period. Beginning in January and following a house to house survey, requirements for screening, including specifications as to the size of mesh, namely from 16 to 18 meshes to the inch, were published, and a definite date set for complete fulfilment. All public buildings at which any gatherings at night would occur, such as churches, were required to install vestibule screen doors. No open-air gatherings were allowed.

For mosquito control operations it was assumed that the area within which operations must be carried on should extend at least one mile beyond the limits of the areas to be protected. This work required the clearing and channeling of the existing waterways, the clearing of old ditches, and the construction of new ditches that were necessary for the draining of swamps, swamp areas, and for the prompt removal of water from the rice fields.

With the commencement of breeding of mosquitoes during the latter part of April, while control measures were instituted, and from that date until the close of the breeding season, all water surfaces within the area, with the exception of the rice fields proper, were sprayed with oil at intervals not greater than seven days.

In 1917 there occurred four deaths from malaria in the control area, against none in this area in 1918. The history incidence index, 29 per cent. or expressed in the number of cases, 522, the only available record for 1917, when compared with the actual development of only one case in 1918, is conclusive proof of the efficiency of the control.

Experiments were made on mosquitoes to determine

how far they fly ordinarily. The experiment consisted of catching, staining, and liberating at a given point *Anopheles quadrimaculatus* mosquitoes and the recatching for examination at given distances from the point of liberation, these distances being at one-fourth mile intervals. The time interval between liberation and the start of recatching was set at thirty-six hours. The question of flight of *Anopheles quadrimaculatus* may be of necessity regarded from two angles, that of experiment and that of observation. In one, the largest experiment of its kind ever undertaken in the United States, there was recorded a flight of one mile. In the other observation there were recorded continuously and on different occasions a flight of one and seven-tenths mile.

It is concluded from this work that malaria has been eliminated from a typical rice field district.

The use of 10 grains of quinine sulphate by mouth for sterilization of the blood of malaria carriers is evidently efficient for one malaria season if used actively over a period of thirty days.

The completely negative clinical history of the nineteen malaria carriers discovered on microscopic examination indicates on the one hand an immense difficulty in obtaining complete malaria control but emphasizes, on the other hand, the importance of the detection of the human carriers.

**Malaria in British Army in Palestine.** This discussion of malaria is a part of experiences recorded by a consulting physician on duty on the Palestine line of communication. This physician was Col. Francis D. Boyd.<sup>6</sup>

In the territory covered by Boyd a large proportion of the medical casualties resulted from malarial infection. While the benign tertian and quartan varieties occurred, the predominant types were primarily malignant tertian and relapsing malaria among the troops who had been infected at other fronts, especially Salonica. By far the most important as affecting lines of communication was the malignant tertian malaria. The onset in these cases was insidious. The patient complained of headache, backache and malaise, with some

---

(6) Edinburgh Med. Jour., May, 1919.

fever, and presented tenderness in the splenic region. There was frequently a history of vomiting. Examination of the blood usually gave a positive finding. But cases occurred in which as many as five examinations had to be undertaken before the parasite was finally discovered. The temperature in these men was usually of a remittent type, ranging from  $104^{\circ}$  to  $102^{\circ}$  F.

A large proportion of the cases showed complications of the most varied descriptions. Prominent among these complications were cerebral phenomena, which varied from slight confusion to an acute maniacal state, and passed rapidly into coma. Conditions presented frequently by the men who developed these cerebral symptoms were hot and dry skin, flushed face, full rapid pulse, sluggish pupils, rigidity of the neck, trismus of the muscles of the jaws, and epileptiform convulsions in some instances. Hyperpyrexia was seen occasionally; in one instance the temperature reached  $109^{\circ}$  F. and was reduced by packs and intravenous injections of quinine. Usually, however, such high temperatures were harbingers of coma and death. Of the more remote effects of malaria on the central nervous system there were seen a number of cases of multiple neuritis, at least three cases of transverse myelitis, with paraplegia and implication of the bladder and rectum.

Abdominal manifestations were relatively frequent. Disturbance of the digestion, with a dry coated tongue, vomiting and jaundice of varying degrees were fairly constant phenomena.

The algid type of malignant tertian malaria at times gave rise to anxiety until a definite diagnosis was established. Some of these severe cases resembled "acute abdomen-perforations." Cholecystitis, appendicitis and other similar conditions were closely simulated in some instances. The pneumonic type of malaria was fairly common among these patients. In such cases, the temperature was irregular and blood examinations showed a malignant tertian infection. Under quinine the temperature fell but the physical signs in the lungs persisted after the fall in the temperature and took a considerable time to clear up. When influenza became epidemic among the troops, pneumonia, following on

influenza, and accompanied by a malignant tertian infection assumed a pronouncedly septic type and was exceedingly fatal. Boyd lays stress on the fact that malignant tertian toxemia has a profound influence on the myocardium. During the acute attacks the blood-pressure may fall low and the heart become dilated: and a certain amount of edema of the lungs may occur.

Renal hemorrhage was rarely encountered. Nephritis following on malarial infections was noted in a number of instances.

Concerning the diagnosis the well-known fact that the parasite must be found in the blood in order to make a positive diagnosis is pointed out. Without positive blood findings, however, in a malarial district, a clinical diagnosis may be fairly based upon: (a) response to quinine therapy; (b) the character of pyrexia, with splenic tenderness and possibly enlargement; (c) the blood-film picture, with the presence of hemozoin-laden leukocytes or a high, large, mononuclear percentage. Given one of these factors present, and the exclusion of other known causes of pyrexia, such as relapsing fever, the diagnosis of malaria seemed justified under conditions where infection was so common.

The causes of death in fifty cases of malignant tertian malaria are shown in the accompanying table:

#### FIFTY CASES OF FATAL MALIGNANT TERTIAN MALARIA

Toxemia with cerebral symptoms.....	10
Toxemia with cardiac failure.....	10
Bilious remittent type .....	7
Hyperpyrexia .....	3
Pneumonia .....	13
Complicated with quartan malaria and bacillary dysentery....	1
Complicated with amebic dysentery.....	1
Complicated with myelitis .....	1
Imperfectly treated .....	4
Total .....	50

Under the heading of treatment, Boyd says that in benign tertian malaria it was customary on the lines of communication after an initial purge, to prescribe quinine doses of from 10 to 15 grains three times a day.

and to evacuate the patient as a cot case if there were no urgent symptoms.

In malignant tertian malaria gastro-intestinal disturbance was so pronounced that intramuscular or intravenous injection of quinine hydrochloride was employed: 12 grains were administered deeply into the muscles of the buttocks three times in the first twenty-four hours, and continued for three days. If by the end of the three days urgent symptoms had disappeared and the temperature had fallen, oral administration was begun, 30 grains being given in twenty-four hours, accompanied with arsenic. During the third week of quinine treatment the daily dose was increased by 15 grains, as it was found that a certain tolerance to the alkaloid had been established. In cases of graver severity treatment was begun by intramuscular injection, followed in two hours by intravenous injection of 6 grains of quinine bihydrochloride.

**Malaria in Macedonia During the War.** A summary of the researches on malaria carried out by French medical officers, with reference almost exclusively to the malaria of Macedonia, is presented by G. Paiseau.<sup>7</sup>

In an attempt to account for the severity of malaria, as seen in this district, he points out that armies in the field obviously place the soldier in such surroundings that he is exposed to particularly virulent infection at a time when his resistance is below normal. There has been much discussion as to what has been the predominant factor in the virulence. Ravaut proved that quinine was administered very unsystematically to patients in the East, and concluded that Macedonian malaria was, above everything, a malaria badly treated. One is compelled, however, Paiseau says, to assign a predominate rôle to the exceptional intensity of the virus in Macedonia during the time when this study was made. He thinks that repeated and continued inoculation and reinoculation have played a predominate part in the severity of type exhibited by the disease.

A serious feature encountered in the work was the resistance of the infection to specific treatment by quinine.

(7) French Supplement to the *Lancet*, May 3, 1919.



In a record of the clinical studies it is stated that in 1916, the earliest cases of primary fever occurred during the second ten days of June. All medical officers were impressed by the severe type of these primary attacks, and all emphasized the violence of onset of the fever, and the variety of pain associated with it—headache, backache, aching legs, profound weakness, digestive and very frequently respiratory troubles, and rapid increase in the size of the spleen.

Certain constant symptoms of malaria were manifested with exceptional severity, as for example, anemia. Paiseau and Lemaire found in addition to the normal type a certain number of rare varieties, such as pseudo-leukemic anemia, pernicious anemia, and certain hemorrhagic forms.

Malarial cachexia is usually the final result of such prolonged infection, but in exceptional circumstances in Macedonia, it was fairly common to find patients dying of premature cachexia after only a few weeks of illness.

The intestinal symptoms were fairly common and were represented by crises of bilious diarrhea accompanying the bouts of malaria.

Peripheral circulatory disturbances were frequent and were observed in all degrees, from erythromelalgia to symmetrical asphyxia of the extremities, passing sometimes into symmetrical superficial gangrene (Raynaud's disease).

During this study, malignant attacks were remarkable not only for their large number, but also for the variety of their clinical forms.

Side by side with the classical comatose cerebral type were to be found other rare varieties, convulsions, coma with hemiplegia, paraplegia, or aphasia; algid types simulating cholera, bilious types, and bilious hemoglobinuria.

It was possible to draw certain conclusions from these facts. The part played by acute adrenal inflammation in the production of the algid type has been demonstrated by the histologic investigations of Paiseau and Lemaire who found, in patients who had succumbed to this variety of the disease, very important lesions sometimes degenerating, sometimes hemorrhagic, of the

adrenal capsules, which at the same time showed a great accumulation of hematozoa.

Meningeal symptoms were sufficiently frequent in malaria for an actual malarial meningitis to be described. Numerous cases of bilious hemoglobinuric fever were observed.

The persistence of complications among malarial patients repatriated from the Balkans have afforded opportunities, especially in France, of studying the secondary complications of the disease. The extent of these have been taken as proof of the insufficient quinine treatment by some authorities.

Complications affecting the sense organs occurred fairly often. Affections of the larynx, paralysis of the muscles of the glottis resulting in aphonia; ocular affections dependent on the nervous mechanism, such as keratitis, iritis, and very frequently hemianopia were observed.

Psychical affections were extremely common among severely affected patients. Psychoses in malaria are always at first confusional in type, co-existing very often with somatic nervous upset, and they occur in patients whose general health is always profoundly disturbed.

A study of the parasitology in this work showed that Macedonian malaria was due almost entirely to the parasites of benign tertian and malignant tertian fever, that of quartan fever being most exceptional.

Concerning prophylaxis in malaria, the author emphasizes that treatment with quinine in this respect is only one of the factors in the fight against malaria, and that by itself it may be insufficient.

No essential change has been introduced in anti-malarial treatment once the disease is developed. The method of intravenous injection he regards as a procedure only for exceptional cases. Intramuscular injections are indicated as the only ones practicable for patients with gastric irritability, who are the subjects of malignant attacks. Concerning the administration of the drug by mouth, he refers to the opinion held by Marchoux as to the value of giving the least soluble forms of quinine, their efficiency being the greater because they are eliminated more slowly. The sulphate.

and above all the alkaloid itself, being more active than other salts. According to Marchoux, chronic malaria must be treated by oral administration.

**Prophylactic Use of Quinine in Malaria.** At the request of Colonel Sir Ronald Ross, the prophylactic use of quinine in malaria is discussed by G. T. Rawnsley.<sup>8</sup>

This author states that during the period which he served in the Twelfth Corps in the British Salonica force, quinine for a prophylactic purpose was given in the following dosage:

1916—5 grains and 10 grains on two successive days in the week, the former amount being more generally employed.

1917—(a) 10 grains on two successive days weekly.

(b) 10 grains on two successive days twice weekly on Wednesday and Thursday and Saturday and Sunday.

(c) 10 grains daily.

(d) 15 grains daily.

(e) 20 grains daily.

The three last amounts were given temporarily to troops a few days before going into, during the period of occupation of, and for a few days after going out of, highly malarial parts of the front trenches.

This dosage completely failed to prevent the incidence of malaria. In one battalion where the large doses of daily quinine were given there was little apparent sickness, the daily dose kept down pyrexia, and the men were thus enabled to carry on with their duties; but after some weeks it was found that these men were affected by chronic malaria as shown by the presence of the parasite in the blood, enlargement of the spleen, anemia, etc., necessitating their admission to hospital in large numbers. It was estimated that at least 80 to 90 per cent. of units were infected.

In 1918, it was decided to give no prophylactic quinine, as the general opinion among the majority of medical officers was that no dose that could be tolerated had any protective value to troops exposed under campaigning conditions. Reliance was placed on other methods of malarial prophylaxis and cases treated as they occurred.

---

(8) Brit. Med. Jour., April 19, 1919.

## TYPHOID AND PARATYPHOID FEVERS.

**The Fate of Typhoid Bacilli in Immune Animals.**

Working in the Laboratory of Pathology and Bacteriology in the University of California, Ruth L. Stone,<sup>1</sup> has carried out experiments for determining the dissemination and destruction of typhoid bacilli injected intravenously in normal and immune rabbits.

She calls attention to the fact that in spite of all that has been accomplished in the prevention of typhoid fever, and of all that has been learned of the nature of the disease, the exact mechanism by which the body is able to protect itself and the manner in which it gets rid of the offending invaders is still unknown. If this could be understood, in a disease such as typhoid where our knowledge of the organism, symptoms, and such are so clear, we might well be able to apply similar deductions to other diseases in which the cause is more or less obscure, and undoubtedly assist the body in its fight to overcome the abnormal conditions under which it is struggling to maintain its own.

With the present knowledge of the typhoid bacillus, its entry into the body, localization in the various organs, and ultimate elimination from these organs, two points of interest suggest themselves to the investigators: First, is there any difference between the normal and immune animal in the length of time that elapses before any or all organs become sterile after intravenous injection of living typhoid bacilli? Secondly, if there is any difference, just what is the mechanism involved, and what factor or factors are responsible for this ability of the immune rabbit so quickly to rid itself of large numbers of living organisms?

Typhoid is a bacteremia, and therefore the bacilli must be carried to all parts of the body by the circulating blood. The question arises as to whether the organisms are killed off simultaneously in the blood and tissues, or remain in the organs after the blood cultures are negative.

By carrying out extensive animal experiments dealing with these questions, the author has established the fol-

(1) Jour. Infect. Dis., October, 1919.

lowing facts concerning the mechanism of bacteriolysis in the body of the immune animal.

Typhoid bacilli disappear more quickly from the organs of immune animals than from normal animals.

Macerated organs taken from immune animals, cut sections or their extracts are not bactericidal even on the addition of fresh immune serum.

Typhoid immune serum is non-bactericidal for typhoid bacilli *in vitro*.

Fresh normal serum is highly bactericidal for typhoid bacilli *in vitro*.

Fresh immune serum *in vivo*, has apparently a high bactericidal power.

Fresh normal serum *in vivo* has no protective power.

This would seem to indicate that the destruction of typhoid bacilli in the immune animal is due either to some interaction between the tissue cells and plasma *in vivo*, or to some other factor which has thus far been overlooked. The theory proposed by Teague, namely, that immunization causes a rapid filtering out of the immune bodies in the capillaries into the tissues, would seem plausible were it not for the fact that the organs of highly immune animals exert no bactericidal action on living typhoid bacilli.

Further work on this subject may lead to more definite conclusions than can here be given.

### **Typhoid Fever Transmitted through Breast Milk.**

This instance of typhoid fever being transmitted through breast milk of the mother is reported by Henry Heiman<sup>2</sup> of New York. The mother was a married woman, 29 years old, whose history aside from the present illness for which she entered the hospital, was negative. She had a typical attack of typhoid fever and the diagnosis was confirmed by the presence of typhoid bacilli in cultures made of the blood and by a positive Widal reaction.

Her child was an infant, 8 months old, whose birth history was perfectly normal. It had been breast-fed until two weeks before the mother was admitted to the hospital, having been weaned because of the mother's illness. There had been no previous illness or previous

---

(2) Jour. Amer. Med. Ass'n, Sept. 20, 1919.



defect. The diagnosis in the child was confirmed by the presence of typhoid bacilli in cultures of the blood and by a positive Widal reaction.

The author considers this experience worthy of report because of its very unusual occurrence. He states that he has been unable to find any similar record in the literature. In one instance, however, reported by Lawrence, typhoid bacilli were found in the breast milk in a nursing mother of 23, ill with the disease, though in that instance the infant escaped infection.

[Perhaps the child was infected from the same source as the mother, *i. e.*: from drinking water or from some other liquid taken by both patients.—B.]

**Antityphoid Serotherapy.** The use of antityphoid serum in the treatment of patients with typhoid fever, is discussed by A. Rodet. The article is a lengthy one, and the use of the serum described in it is summarized by Lodilla Ambrose<sup>3</sup> of New Orleans.

In this summary, it is stated that when the serum is administered soon enough (in the absence of established complications), in sufficient doses, and at suitable intervals, in the majority of cases it prevents the progress of the intoxication, attenuates the toxic disturbances already existing, initiates defervescence and, finally, the duration of the disease.

In order to have its full effect, the serum ought to be given before the eleventh day of the febrile period. Later, the useful effects are far from being always *nil*, but they are inconstant and generally less pronounced.

The treatment ought to begin by a relatively strong dose, from 15 to 20 c.c. This dose may be repeated, but very often one may content himself with decreasing doses (from 10 to 5 c.c.). As a rule, three injections suffice, sometimes two; a fourth may be necessary. The interval between the injections which seems the most suitable is forty-eight hours.

The influence of the serum on the thermic curve sometimes becomes evident beginning with the day following the first injection, oftener after thirty-six or forty-eight hours; sometimes it is delayed until the second injection, more rarely until the third. It is the initial stage of the

(3) New Orleans Med. and Surg. Jour., June, 1919.

defervescence, which is then continued according to the different types.

In quite a large proportion of cases, when the serum intervenes soon enough, the lowering of the temperature is rapid and regularly progressive in such manner as to attain apyrexia in from six to eight days; this "aborted" type, to use the expression of Etienne, may be observed even after a very severe onset. In other cases, the defervescence lingers at an average thermic level inferior to that of the onset, and generally then with amplified diurnal oscillations. More rarely, after a more or less marked lowering, the temperature curve rises, then continues at that level. This type (the type "*a encoke*" of Etienne) is seen especially in the cases of late treatment: in its way it bears witness in favor of the serum, putting in evidence, a temporary specific action.

Parallelling the modifications of the thermic curve, the other symptoms improve, more particularly those which betray the toxic involvement of the nervous system, the violent headache, the prostration, the cardiac asthenia. Very frequently this improvement precedes defervescence: sometimes the first effect of the serum is a relative well-being, beginning with the first hours after the first injection, and on the following days one often observes a veritable euphoria (even though the temperature lags in lowering), and the disease progresses with a minimum of toxic disturbances.

The recrudescence and the relapses are not rare. Far from constituting an argument against the serum, they plead rather in favor of a specific action, either incomplete or insufficiently prolonged. The one and the other could without doubt be avoided or combated, either by a better regulation of the dosage according to the case or by a repetition of the treatment.

In order that the serum may have its complete effect it is necessary that the typhoid infection should be free from every secondary infection. The pre-existence of advanced tuberculous lesions, a simultaneous or secondary infection (streptococcus, staphylococcus, diphtheria bacillus, etc.) restricts its efficacy.

**Typhoid After Prophylactic Inoculation.** Of recent years typhoid fever in the United States Army has been

conspicuous by its rarity. It is shown in this report by C. P. Brown, F. W. Palfrew, and L. Hart,<sup>4</sup> of the Medical Corps, U. S. Army, that while rare typhoid can not be considered as non-existent. In cases of continued fever, it is still to be suspected, and even more important, the protection of prophylactic inoculations, great as has been their service, cannot be taken as absolute to such an extent that sanitary precautions can be neglected.

These authors observed that during the latter part of June, 1918, cases began to appear at the Base Hospital at Camp Greene, N. C., which from their gradual onset, climbing temperatures, without evidence of local inflammatory disease, enlarged spleen, rose spots and leukopenia, presented the clinical picture of typhoid fever. The suspicion was verified, and eighteen soldiers at this camp developed the disease, beginning at the date mentioned above. That these were undoubted cases of true typhoid fever is shown conclusively by the clinical history, the physical findings and the laboratory results obtained from cultures of blood, urine and feces.

A careful investigation showed that it was unlikely that the failure of immunity was due to failure to receive the standard vaccine in standard doses.

Much more strongly suggested was the exposure of these patients to massive doses of the infective agent, against which the immunity produced by the standard process of vaccination was inadequate. Most of the cases occurred in a short period of time, coincident with a mild epidemic in the nearby city of Charlotte. Most of them occurred in one organization. While no conclusive source of infection was proved, the assumption was warranted that some source of marked virulence existed.

According to these authors it is to be concluded, therefore, that occasional cases occur in which the usual preventive inoculations against typhoid fever fail to protect against the disease, most probably on account of the ingestion of virulent organisms in massive doses. To eliminate such occurrences, sanitary precautions should prevail; but they can succeed only by constant attention to the guarding of food and drink against contamination.

(4) Jour. Amer. Med. Ass'n, Feb. 15, 1919.

Serious contaminations of water-supply and of milk on a large scale near the source can ordinarily be prevented by the efforts of sanitary officers, civil and military, working in coöperation. The contamination of water, ice, milk and food on a smaller scale by carriers among food handlers, and by flies, however, is a matter that demands more laborious and detailed attention. Success in the protection of latrines and in the control of flies is never absolute, but only relative and in proportion to the care devoted to the subject.

No false sense of security from typhoid vaccination should be permitted to relax vigilance in this direction. But more important still is the supervision of food handlers, not only to insure cleanliness, but also by bacteriologic tests of each individual to exclude the admission of a carrier to any position from which he can contaminate the food or drink of his company. It is to be realized, moreover, that a single bacteriologic test, if negative, is not absolute protection, as illustrated by the number of negative feces examinations even in acute cases. Inquiry should therefore be made in all cases as to typhoid fever in the past, and when positive or suggestive history is found, the person should be excluded from handling food until repeated cultures have proved negative. More difficult even than the control of the company mess is the supervision of restaurants and lunch counters outside of the camp. The only way of preventing danger from such sources is to prevent soldiers from taking food or drink outside of their own mess, whenever typhoid fever is known to be present in the neighborhood.

[The Editor agrees with the conclusions of the authors. There can be no doubt that in certain epidemics, the strain of typhoid bacteria may be so virulent, that the temporary acquired immunity obtained by prophylactic inoculation given with approved technique and standardized vaccine is not sufficient to protect the individual. It is also true that this fact does not in any way detract from the value or the utility of prophylactic typhoid inoculation. It does mean alertness in the enforcement of general hygienic and other antityphoid precautions.—B.]

### **Typhoid Fever Among American Troops in England.**

While the subject of typhoid fever is not an extensive one in the present day literature, an account of an interesting experience with this disease is recorded by C. B. Hawn, J. D. Hopkins and E. M. Meader,<sup>5</sup> of the Medical Corps of the U. S. Army.

The article deals with an outbreak of typhoid fever among American troops in England. The organization left Camp Cody, in Deming, N. M., June 15, 1918, for Camp Merritt, N. J. While *en route*, June 18, the organization stopped at Meridian, Miss., and was taken for a swim in a lake. The organization arrived at Camp Merritt June 21, embarked June 28, and arrived at Liverpool July 10.

From a study of the history of each case, that developed typhoid among these men, it was noted that the date of onset varied over a period of about one month. The first patient was ill on leaving Camp Cody. A total of ninety-eight cases finally developed among a group of 248 men.

A careful study brought out the fact that a considerable group of cases developed the latter part of June and the early part of July. This suggests a common source of infection. Two possibilities presented themselves. These patients became infected either in the train early in the journey, or by bathing in the water at Meridian, Miss., June 18. The water may easily have been infected by one or two typhoid patients who were present in the organization at the time. In the remaining cases of typhoid, the men undoubtedly received their infection by contact with the patients who were ill in the organization. This could easily have been done, since the men were crowded together on the train, or on shipboard. All these patients had been inoculated with either typhoid vaccine or paratyphoid vaccine or triple typhoid vaccine, or both. Many of them had received several doses in excess of the required number, and the men were inoculated at widely different posts and at different times. One patient stated that he had received but one dose. Otherwise, it would seem that the whole organization was thoroughly immunized.

(5) Jour. Amer. Med. Ass'n, Feb. 8, 1919.



The following summary of laboratory findings in studying these patients is presented:

#### SUMMARY OF LABORATORY FINDINGS

	No. of Cases
<i>B. typhosus</i> isolated from blood and from stool.....	4
<i>B. typhosus</i> isolated from blood only.....	8
<i>B. typhosus</i> isolated from stool only.....	5
Typical typhoid lesions at necropsy in cases in which the bacillus was not isolated during life ( <i>B. typhosus</i> isolated postmortem from two of the foregoing).....	3
Typical shift in typhoid agglutinins; blood and stool cul- tures negative .....	6

Blood cultures in sterile ox bile yielded positive results in about 30 per cent. of the cases. This is higher than would be expected when it is considered that most were cultivated in the third week or even later in the disease.

In commenting upon this situation, the authors state that the most interesting question that arises here in regard to these cases is why did this large group of vaccinated men become infected? To this three possible answers present themselves: First, that the vaccination was defective; second, that the infection was due to the abnormal race of *B. typhosus* against which the vaccine did not protect, and third, the men received an overwhelming dose of the infecting organism.

In the absence of evidence that the prophylactic immunization of these men differed in any way from that which has in the vast majority of cases given adequate protection, or that the strains of typhoid with which they were infected was atypical, there remains the hypothesis that they received an excessive dose of typhoid bacilli.

[See editorial note on preceding article.—B.]

Conclusions drawn from the report are as follows:

Owing to the lateness of the course on admission to the hospital, cultural confirmation of clinical diagnosis was impossible in a considerable number of cases. The fact that all these men had received routine immunizing vaccine during the past eleven months made the ordinary Widal reaction unreliable. Careful clinical study.

however, justifies a positive diagnosis in thirty-eight of the cases.

That severe typhoid may occur in vaccinated men is proved by this series of cases.

The occurrence of uniformly low white blood counts in this series again illustrates the diagnostic value of routine blood examination in all febrile conditions.

The authors feel that the atropine test may be of great value in the diagnosis of typhoid fever, although the smallness of this series, the impossibility of laboratory confirmation of diagnosis, and the lack of control cases makes authoritative conclusions in this matter impossible.

It is hoped that the explanation of the lamentably high mortality rate (13.15 per cent.) may be found in the average lateness in the course of disease on admission to the hospital.

**A Third Form of Paratyphoid.** Lewy and Schiff<sup>6</sup> in confirmation of observations by other workers in Syria, Palestine, Mosul, Albania, and Wolhynia, describe a febrile illness associated with infection by a bacillus of the paratyphoid group. The bacillus, which has been named *B. erzindjan* by Neukirch and has been separately discovered by Weil, gives the cultural characteristics of *B. paratyphosus*, but different agglutinations. The disease is sometimes associated with diarrhea, but the most striking feature is the severity of toxemic symptoms. The temperature is high, sometimes simulating the curve of typhoid, the pulse is relatively slow, rose spots are not observed. The fever is commonly of long duration and the mortality, except in natives of the districts, is high. The bacillus, the authors state, can be cultivated from the blood, with ease and regularity. Postmortem abscesses are commonly found in the skin, and in the liver and kidneys, and there may be hemorrhages in the serous membranes. The spleen is enlarged. Typical intestinal ulceration is not found. The disease is much more of a septicemic type than is commonly seen in the enteric group of infections.

(6) Berlin. klin. Wochschr., Nov. 10, 1919.

## DYSENTERY

**Dysentery—Bacillary and Amebic.** In an investigation of bacillary dysentery carried out by L. S. Dudgeon and his associates, 145 cases had blood cultures done during the acute stages of the infections. In only two of these cases were the dysentery bacilli found by blood culture. In carrying out bacteriologic investigations of the stools in acute and chronic bacillary dysentery, the stools were obtained in the fresh state, and experimental evidence was obtained, which showed that an additional volume of 3 per cent. of normal sodium hydrate to pure blood and mucus stools at the time the specimens were collected from the patients was a distinct advantage, and still more so if the dysenteric stools contained fecal matter. A higher percentage of positive findings occurred when it had been necessary to delay the bacteriologic examination for some hours.

The strains of Shiga bacilli isolated during this work did not call for any special comment. Two types of para-Shiga bacilli were isolated. These were differentiated by serologic tests and by the fact that the group designated para-Shiga + produced indol, while the para-Shiga bacillus failed to do this. Organisms of the Flexner group were encountered and Dudgeon states that there is no justification for the rejection as a cause of dysentery of the bacilli which retain the primary cultural characteristics of the Flexner group for five days if they do not agglutinate with the available anti-serums.

Other phases of this investigation bring out the fact that bacillary dysentery is most prevalent when flies are most numerous. Flies after contact with food infected with dysentery bacilli are capable of carrying and disseminating these bacilli for at least twenty-four hours. Dysentery bacilli were isolated from wild flies captured in places in which bacillary dysentery was both endemic and epidemic.

In the opinion of Dudgeon and his associates, the following points require much more elaborate investigation: (a) The vitality of dysentery bacilli in water:

(S) Brit. Med. Jour., April 12, 1919.

(b) the relationship of flies to bacillary dysentery; (c) further investigation with the Flexner group of dysentery bacilli and with inagglutinable strains of Flexner bacilli; (d) study of the toxin produced by dysentery bacilli; (e) preparation of more suitable antiserums for treatment of the disease.

**Amebic Dysentery in Britain.** A continuation of this work is presented by Warrington Yorke,<sup>9</sup> Professor of Parasitology, University of Liverpool, who has made a study of amebic dysentery in England. In all, over 4,000 chronic or convalescent dysenteries were examined at the Liverpool School of Tropical Medicine; *E. histolytica* was found in about 7.5 per cent. of cases. It is clear to this author that there is a considerable percentage of individuals infected with *E. histolytica*, among persons who have never been out of Great Britain. It is his view also that at present there is no character by which it is possible with certainty to distinguish the vegetative stage of *E. histolytica* from the corresponding stage of *B. coli*. He therefore suggests as a general guide that if endamebas are found in numbers in the stools of a person suffering from acute or subacute dysentery the case should for purposes of treatment be regarded as one of amebic dysentery. *B. coli* may be present in the beginning of an attack of bacillary dysentery, but as the dysentery continues the colon bacilli rapidly disappear.

Yorke gives details for the treatment of this disease as follows:

A preliminary saline purge is given unless the acute dysentery has already persisted for several days, in which case it is unnecessary. Emetine hydrochloride, 1 gr., is injected subcutaneously and bismuth subnitrate (2 or 3 drams suspended in milk or water) is given by mouth three or four times daily for a period of twelve days.

Occasionally a morning saline may be necessary if the bismuth causes constipation.

This treatment invariably clears stools of the entamebae, a result which can by no means be claimed for emetine alone, and causes the disappearance of acute

(9) Brit. Med. Jour., April 12, 1919.

dysentery, the stools speedily becoming less frequent and free from blood and mucus.

**Dysentery in British Army in the East.** Prominent among the diseases encountered by Col. F. C. Boyd,<sup>1</sup> while acting as a consulting physician on duty on the Palestine lines of communication, was dysentery.

He says that as in all campaigns in the East, dysentery, both bacillary and amebic, has bulked largely as a cause of sickness in the army in Palestine.

In the bacillary type both the classical types, namely, true Shiga and the Flexner-Y strain were frequently isolated. The treatment of the bacillary type was as follows: dietetic, serum therapy and the administration of saline.

The diet most suitable for these patients was found to be albumin water, beef and chicken tea, meat-jelly, barley water, sweet tea without milk, and arrowroot.

He considers that the serum treatment was undoubtedly successful, but two factors are necessary for success: First, that it be given early, and, second, that it be given in sufficient doses.

In this work all patients suffering from diarrhea with blood and mucus in the stools were given a dose of serum whenever they came under treatment, without waiting for a laboratory diagnosis: the minimum dose was fixed at 80 c.c. The saline treatment was undoubtedly helpful; sodium sulphate being given in gram doses at first every four hours, and diminished when the stools became feculent. In this work amebic dysentery was not so prevalent as the bacillary form, yet, it led to a considerable amount of illness, especially among the troops reporting sick in the Jordan Valley.

In cases of amebic dysentery, granted that a correct diagnosis had been made, treatment with emetine was found to be very satisfactory. The doses of emetine employed was usually  $1\frac{1}{2}$  grain twice daily by hypodermic injection for thirteen days. A number of cases of abscess of the liver occurred and were treated surgically. In most of the cases of this kind there was an entire absence of any history of dysentery. The abscesses occurred in carriers who had not suffered from

(1) Edinburgh Med. Jour., May, 1919.



an acute attack. Mixed infections of bacillary and amebic dysentery were by no means uncommon among these troops. It seemed as if these individuals had been ameba carriers who had become infected with bacillary dysentery, by which the intestinal resistance had been lowered and amebic dysentery developed.

### **Epidemiology and Treatment of Amebic Dysentery.**

In the transactions of the Clinical Society of the University of Michigan, there is recorded a note concerning the epidemiology and treatment of amebic dysentery, with the report of two cases, by G. R. Herrmann.<sup>2</sup>

The occurrence of these patients suffering with amebic dysentery in the medical clinic of the University Hospital at Ann Arbor, brought up two questions of vital importance along the line of public health for the future.

The questions were: First, is the disease transmitted by carriers? and, second, are there sporadic cases arising in the north temperate zone? A careful examination of the history of each of these patients does not produce conclusive evidence but there is quite a considerable pointing toward the long latent carrier idea in them. Two cases are not sufficient grounds from which to draw any conclusions. The author takes the position that the cases agree with the most recent ideas concerning the disease. At any rate, whether carrier, latent contact, or convalescent, or whether sporadic, indigenous cases, they should serve to put physicians on their guard that they may early solve the problem and prevent the development of a serious epidemic.

Under the heading of treatment, Herrmann gives a brief review of literature on this subject, and the various methods of treatment recorded, deal with the use of quinine, emetine hydrochloride, emetine-bismuth-iodine, and ipecac.

In the two cases here reported the patients were put to bed at complete rest. The bowels were cleaned with calomel and salts, and  $1\frac{1}{2}$  gr. emetine hydrochloride was given three times a day subcutaneously. At the same time, 60 grains of ipecac powder in salol-coated pills were given daily as a single dose before sleeping time in one case, and in divided doses of 20 grains before

(2) Jour. Mich. State Med. Soc., January, 1919.

meals in the other case. The ipecac was gradually reduced by 5 grains a day, and the emetine hydrochloride was stopped after ten days. Since these were both chronic cases, in which there were probably partly healed ulcers and pockets in the colon mucosa and wall, which would lodge cysts of the endameba and protect them from action of a drug in the circulation alone, a combination of drugs was resorted to.

This method of administration was satisfactory, and the results were apparently excellent.

Herrmann feels that the main virtue of the modern treatment lies in the attack on the organism in the bowel itself where it is lodged. The active principle of the drug when brought to the parts by the circulation is not able to reach encysted forms, which are buried in scar tissue, or sloughing pockets in colonic mucosa. Both ends may be accomplished by the combination, the oral administration would strike from the lumen, while the subcutaneous injections made sure that beginning metastatic foci outside the alimentary canal would not escape medication.

The use of emetine-bismuth-iodide is said to make the subcutaneous injections unnecessary.

#### **Mixed Treatment of Chronic Intestinal Amebiasis.**

In a treatise on this subject, Ravaut and Charpin<sup>3</sup> report five cases of amebic dysentery under treatment with emetine injections during a period from six to sixteen months. Although there was an initial improvement under this treatment, there were numerous recurrences; and negative results were also obtained under this mixed treatment.

The authors advocate the administration of the drugs by mouth in the chronic cases. Intravenous and subcutaneous medication is reserved for the acute and subacute cases, and for those with hepatic complications. They employ the double iodide of emetine and bismuth in doses of 0.18 grams daily. Larger doses are not tolerated by the weak on account of the cramps, diarrhea and circulatory and renal disturbances. The combination of remedies which the authors found most efficacious in the five intractable cases was neosalvarsan by mouth

(3) Paris méd., August, 1919.

in 0.1 gram gluten-coated capsules, and a paste consisting of 100 grams each of powdered charcoal, powdered bismuth subnitrate, syrup and glycerine together with four grams of powdered ipecac. In cases in which there is violent and painful diarrhea 0.8 grams of powdered opium may be added. Each dram of this combination contains 0.1 gm. ipecac. From two to ten teaspoonsful of the paste is taken daily, alternating with neosalvarsan capsules (one or two).

The authors state that with this treatment, no nausea, vomiting, diarrhea or cramps was caused in any of their five patients. The general condition rapidly improved and the amebas were soon destroyed. As a supplementary treatment, enemas of from 0.15 to 0.3 grams neosalvarsan in 100 c.c. of water with a small quantity of extract of opium were employed.

**Vaccine Therapy in Bacillary Dysentery.** This article by P. Nolf,<sup>4</sup> of Brussels, deals with bacillary dysentery and its treatment among Belgian soldiers. In 1918, especially during August and September, over 500 cases of bacillary dysentery were encountered by the author and his staff. About 20 per cent. of these were severe or very serious cases, and 80 per cent. were light or moderately severe cases. Among these patients, as among some seen by Nolf in 1917, who suffered with a similar disease, there was a marked predominance of Flexner bacillus and bacillus Y; in fact, the Shiga bacillus was not isolated in any case, and in only three instances was agglutination of the Shiga germ obtained. In all three of these there was also agglutination of the Flexner bacillus in high dilutions.

From the viewpoint of symptomatology, the 100 serious or very grave cases could be divided into two nearly equal parts, one half being choleric. These were the cases in which the diarrhea was accompanied by vomiting, which not only increases the loss of fluid from the body, but also prevents its restoration by the ingestion of liquids. In a certain number, the vomiting came on early, appearing very shortly after the first diarrheal evacuation.

The treatment consisted of subcutaneous administra-

---

(4) Jour. Amer. Med. Ass'n, Oct. 18, 1919.

tion of from one to two liters of isotonic saline together with a fluid diet. Frequently after twelve hours the appearance of these patients was much improved and in a few days definite cure followed. In view of his experiences in the 1917 epidemic, combined with those of the 1918 epidemic, Nolf states that he is seriously tempted to affirm that in the choleric form of bacillary dysentery improvement tends to be rapid provided the dehydration is combated from the beginning.

In the other half of the serious cases there was no suddenness in the onset, no dehydration, no collapse; but the gastro-intestinal disturbances were more resistant. The stools were persistently liquid with mucous or abundant muco-pus and blood. There may, indeed, be hemorrhage of dangerous magnitude.

Specific serotherapy proved futile in the treatment of these cases of dysentery, therefore, toward the end of the epidemic in 1917, Nolf employed vaccine therapy in the chronic cases that remained. When possible to isolate a dysentery germ from the intestines, there was made and employed an autogenous vaccine; otherwise a vaccine of a Flexner bacillus type made from a gelose culture killed by heat was used. The vaccines were administered subcutaneously at first in progressively increasing doses, the initial dose being usually 10,000. To obtain the desired results it was necessary to raise the dose frequently from five to ten million. During the later part of the work in 1917 some vaccines were administered intravenously. The successes obtained then induced Nolf to try the intravenous method in a number of the cases of acute dysentery in the summer of 1918. The doses were given at four-day intervals, the initial dose being regularly 10,000 germs, then 30,000, then 50,000, then 100,000, etc. In general, the betterment of the patient did not long delay. The fever dropped by lysis, with some recrudescences more or less marked on the days of vaccine therapy, and the next day, and the intestinal symptoms improved coincidentally. In many cases of moderate intensity a complete cure was effected when the dose of 500,000 was reached. In the more refractory cases, it was necessary to push the vaccine up to about 10,000,000.

In fifty-two cases treated thus intravenously, there were only two deaths. By this method of vaccinothrapy the dangerous tendency toward chronicity which was produced in a considerable number of the patients in 1917 was avoided. This result is considered by Nolf particularly gratifying.

A complete record of the epidemic of bacillary dysentery of 1918 shows a complete cure at the latest in a few weeks' time in 500 cases, excepting only two patients who died and two who left before the cure was completed. The author has not had occasion to try this method in patients with Shiga bacillary dysentery and is therefore not willing to speak of its utility in that form of the disease. In acute dysentery, he says, intravenous vaccinothrapy cures quickly in cases exhibiting protracted fever and lasting diarrhea with hemorrhagic and slimy stools, these being the cases that are refractory to other therapeutic methods, including serotherapy.

**Treatment of Chronic Amebic Dysentery With Double Iodide of Emetine-Bismuth.** J. Carle<sup>5</sup> remarks that while emetine is very precious in the acute form, it is without action when the amebas are encysted. In a series of thirty-five chronic cases treated by the usual methods he had many failures; he then treated another series, of twenty-five, with the double iodide. The patients all had the chronic type, in fact one had had symptoms for eighteen years, and another for seven years. The general condition was grave—marked emaciation, feebleness, gastric disturbances, and permanent or intermittent diarrhea. In all, proctoscopy showed an abnormal state of the mucosa, from simple edema to ulceration.

The course was that advised by Metz—a keratin-coated pill of the drug, 0.06 gm. at the three meals for twelve days. In spite of the coating of the pills, nausea and vomiting are common; but these symptoms last, as a rule, only two or three days, often reappearing for the last few days of the course. The diarrhea is always exaggerated or provoked by the treatment, here again it is at the beginning and close of the course; it should be

(5) Archiv. d. mal. de l'app. digestif, July, 1919.



checked with opium only when too intense. As is the case with the emetine alone, the double salt may produce untoward effects, hence it should always be associated with cardiac tonics, camphorated oil, adrenalin, etc.

The following summary is presented:

1. Simple chronic amebiasis rarely resists the action of the double iodide. A man who contracted the disease (in Cambodia) in 1900, was definitively relieved of his cysts after a course of twelve days. Moreover, the cure was speedy in twelve of the twenty-five cases.

2. Cure is exceptional when animal parasites (*Trichomonas*, etc.) are associated. After these are got rid of, which is easy, except for *Giardia (Lamblia)*, a new course of the double iodide leads to cure.

3. Recovery may be delayed by the condition of the gastro-intestinal canal—secretory insufficiency, intestinal fermentation, enteroneurosis. Hence in addition to the amebiasis itself, the general and psychic condition must be looked after.

Relapses have been noticed for from four to six months after apparent cure; hence the course should be repeated at intervals not too far apart. Should there be association with other parasites, a double course of treatment is to be instituted again.

**Protozoölogic and Clinical Studies on the Treatment of Protozoal Dysentery With Benzyl Benzoate.** An investigation of the pharmacologic action of two esters, benzyl acetate and benzyl benzoate was made by Macht at the Johns Hopkins University. The drug was applied there with apparent success in the treatment of a patient who suffered with endamebiasis of fifteen years' standing. Knowledge of this work led the authors, F. G. Haughwout, P. T. Lantin and M. A. Asuzano,<sup>6</sup> to test this drug in the treatment of dysentery in the Philippine Islands. Ten cases were studied by the first two authors named. Eight of these were endamebic without complications, such as infection with *Bacillus dysenteriae*. One patient suffered with *Bacillus dysenteriae*, and one other with miliary tuberculosis.

The diagnosis in each of these instances was as accu-

---

(6) Archiv. Int. Med., October, 1919.

rate as could be made using bacteriologic and microscopic methods. Concerning the character of the stools of these patients, the authors regarded as suspicious of bacillary dysentery a stool that was found to be rich in cellular exudate, mostly of a polymorphonuclear nature, one that is strongly indicative of an acute inflammatory process and of toxic necrosis. Stools of the latter type are often found to contain *Endamoeba dysenteriae*. In such cases it is customary to regard the condition as probably one of mixed bacillary and endamebic dysentery infection. The authors are not in accord with those who hold that endamebic dysentery does not become complicated by invasion of the amebic ulcers in the intestinal wall by bacteria other than *Bacillus dysenteriae* with consequent evidence in the stools of an acute inflammatory process. Much weight is given to the statement made by Cowan and Miller that they doubt the existence of pure endamebic infection as they are skeptical of the existence of chronic bacillary dysentery. It is this factor that seems to inject an element of doubt into the otherwise apparently reliable method of cytodagnosis as employed in dysentery.

Concerning the treatment of patients in this work, it is said that as a routine measure, all patients received aperient sulphates. In some instances, enemas of potassium permanganate were given to clear out the bowel when the stools were formed. Ipecacuanha when administered was given in the form of salol-coated pills. The dose on each of three successive nights was 180 eg. In acute cases 4 eg. of emetine hydrochloride were given daily hypodermically. When the acute symptoms subsided this dose was reduced to 2 eg. daily. In very severe cases a combination of ipecac, emetine and benzyl benzoate may be employed.

Pending diagnosis it is the custom of the authors in fulminating dysentery to administer serum at once. Because of the acute and rapid course severe bacillary dysentery runs it is considered best to give the serum liberally without waiting for the laboratory report. It can do no harm and may do a great deal of good, for it is the experience of one of the present workers that the serum treatment achieves its best result when applied

early in the attack. Much caution is used in the application of emetine in undetermined dysentery because of its mischievous effects on the heart that may be impaired in bacillary dysentery.

Benzyl benzoate was administered in a small amount of cold water three times a day after meals. The doses employed varied from 20 to 30 drops of the 20 per cent. alcoholic solution.

In these eight patients with uncomplicated endamebic dysentery who were given benzyl benzoate, good results were noted in each instance. All these cases were of the acute type and varied in severity. The action of the drug in chronic cases and in carriers has not been tried. No ill effects on the alimentary or excretory tracts following the administration of benzyl benzoate were observed. In no instance did the drug alter unfavorably the course of a disease. On the contrary, its administration was accompanied in each case by a marked alleviation of both the objective and subjective symptoms of the disease. It was found to give the patient much needed rest and permit him to sleep at night, a most important desideratum in the treatment of dysentery. It was found to shorten the term of illness, noticeably. In some of these patients benzyl benzoate alone was observed to bring about a complete subsidence of acute endamebic dysentery.

The authors considered it, therefore, a valuable auxiliary to the other forms of anti-amebic treatment and think that it offers real promise of usefulness when employed alone. This is entirely aside from any amebicidal powers that it may in the future be shown to possess. They state further that benzyl benzoate seems to take the place of morphine in dysentery in that it slows the peristalsis and relieves the pain and tenesmus, but shows none of the undesirable traits of opium.

As an addendum to this report there is the record of the treatment of two patients with amebic dysentery by M. A. Asuzano. The treatment included the administration of emetine bismuthous iodide, and later emetine hydrochloride, but under it little, if any, improvement was noted in the symptoms. Later, emetine hydrochloride was combined with benzyl benzoate in one instance,

and complete and speedy subsidence of all the symptoms and the disappearance of the parasites from the stool followed immediately.

To the other patient no emetine was given. Under treatment with benzyl benzoate alone the symptoms rapidly disappeared, and with them, the endamebas in both the trophozoite and the encysted forms disappeared. The question of how long endamebas were absent from the stool and of how long the clinical symptoms of the disease are disposed of by the use of benzyl benzoate must remain in doubt until there is further time for observation and for the treatment of more patients.

**Treatment of Carriers of Amebic Dysentery.** M. Labbé<sup>7</sup> in several hundred patients made systematic tests of the various treatments proposed: Most of the subjects were simple carriers of cysts with a non-dysenteric diarrhea. A few in the beginning, had living amebas, these latter sometimes reappeared during the treatment.

As a rule the *modus operandi* was: Three days of emetine hydrochloride 6 to 8 cg.; one day of neo-arsenobenzol, 0.15 to 0.20; at the same time, enemas of 1:1000 nitrate of silver. At the end of eight days, the stools were examined, if amebic cysts were still found, a second course of treatment was given. If cysts were absent, the patient was left at rest for eight days, when another examination was made. If the cysts were again present, treatment was recommenced once more; if not cure was concluded and the patient discharged.

It took from seven to 180 days for the cysts to disappear. The patients were given doses of emetine varying from gm. 0.36 to 1.68 and even 2.96. These amounts were well borne.

In seventeen instances, the double iodide of emetine and bismuth was administered either alone or in conjunction with the emetine hydrochloride. The effect did not seem any better than that from emetine alone, but Labbé adds it is only fair to state that the double salt was used mostly in rebellious cases, and that in cases especially stubborn to the emetine, the cysts disappeared in from ten to fifteen days.

---

(7) Archiv. d. mal. de l'app. digestif. July, 1919.

Arsenobenzol intravenously did not seem to exert any clear action on the cysts.

The enemas with silver nitrate were usually well borne, if too irritating, they can be replaced by permanganate or peroxide.

Labbé concludes that the mixed treatment persevered in will cause disappearance of the cysts, this may take several months, and occasionally is not permanent. Therefore patients should be kept under supervision.

**A New Form of Endameba.** A new form of endameba with criterions for distinguishing the endameba of amebiasis from other organisms are reported by C. A. Kofoid, S. I. Kornhauser and O. Swezy.<sup>8</sup> The new organism is called *Endamoeba nana*, and is said to be apparently a non-pathogenic species, and perhaps the most common intestinal ameba among American troops. The figures indicate that of 1,500 men in America and overseas, 417, or 28 per cent., were found to pass the organism in their stools while only 389 of the 1,500, or 23 per cent., passed *E. coli*., and 139, or 9.3 per cent., passed *E. dysenteriae*.

This new organism was found to have a wide geographic distribution, and therefore will be encountered frequently by those who make examinations of stools, even in America, and the examiner must be prepared to distinguish the *E. dysenteriae* not only from the well known *E. coli*, but also from this new organism, *E. nana*.

In discussing free stages of ameba, the authors state that in cases of acute amebic dysentery the large free *E. dysenteriae* are readily distinguished from *E. coli*, by their ingested red blood corpuscles, their clear hyaline pseudopodia, and their very active locomotion. *E. coli*, rarely ingests the corpuscles, has granular pseudopodia and is sluggish in movement. There is an absolutely diagnostic criterion for the separation of the free stages of *E. dysenteriae* from those of *E. nana*.

In *E. dysenteriae* (Fig. 3.—1 to 11) there is a central karyosome and the peripheral chromatin is scattered over the nuclear membrane somewhat uniformly in plaques or granules of small size. In *E. nana* (Fig. 4.—12 to 23) there is no central granule and the peripheral chromatin

(8) Archiv. Int. Med., July, 1919.



is massed in a single large clump at one point on the nuclear membrane. These nuclear contrasts may sometimes be made out in the living material or in iodine-eosin, but are perfectly distinct in amebas stained in iron hematoxylin (Fig. 5—24 to 28).

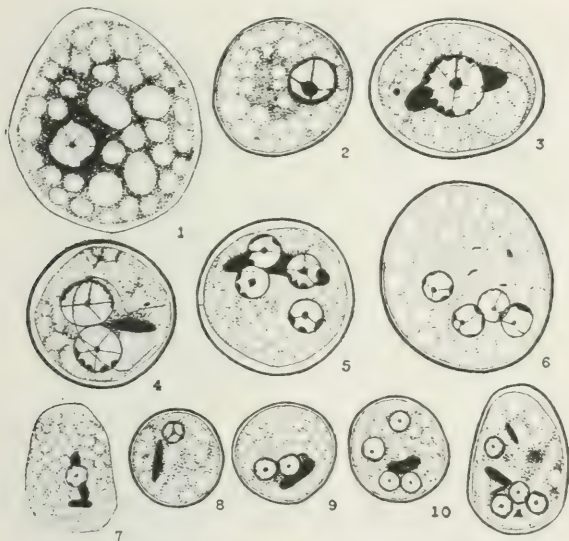


Fig. 3.—1 to 6.\*—Large races of *Endamoeba dysenteriae* (10-17 microns) stained with iron hematoxylin.  $\times 2800$ . (1) Relatively small, free ameba in contracted condition, showing clear, peripheral ectoplasm; 17 microns. (2) Mononucleate cyst with peripheral chromatin uncontracted and no chromatoidal body; 10 microns. (3) Same, with large, stout chromatoidal rod; chromatin on nuclear membrane gathered in small clumps; large glycogen vacuole in cytoplasm; 10 by 13 microns. (4) Binucleate cyst with small fusiform chromatoidal rod and slender, coiled thread; 11 microns. (5) Quadrinucleate or tetragenous cyst with large chromatoidal rod; 12 microns. (6) Largest race of *E. dysenteriae* four nuclei; no chromatoidal rod; 14 microns.

7 to 11.—Small races of *Endamoeba dysenteriae* (7-10 microns) stained with iron hematoxylin.  $\times 2800$ . (7) Small, free ameba evidently approaching encystment; two chromatoidal bodies; 7 by 10 microns. (8) Small mononucleate cyst with slender chromatoidal bar; 7 microns. (9) Small binucleate cyst with two chromatoidal bars; 8 microns. (10) Small quadrinucleate cyst with stout chromatoidal body; 8 microns. (11) Ovoidal cyst with four nuclei and three chromatoidal bars; 7 by 11 microns.

\* All drawings have been made by Dr. Olive Swezy under a grant from the Division of Medicine and Related Sciences, National Council of Research.

In considering encysted stages of amebas, the authors say that in cases of chronic and latent intestinal amebiasis, and in carriers, the evidence of infection will be determined mainly by the encysted stages which occur in formed stools, or in the semi-fluid ones, which often

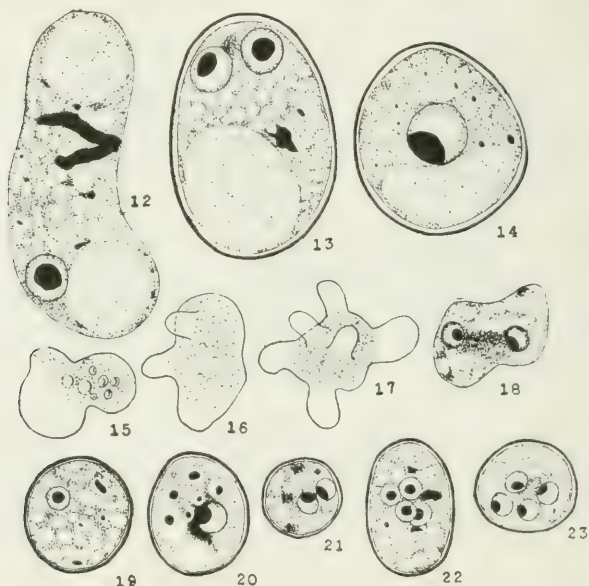


Fig. 4.—12 to 14.—Large race of *Endamoeba nana*, stained with iron hematoxylin,  $\times 2800$ . (12) Sluggish, free ameba from formed stool, mononucleate with two empty glycogen vacuoles, a large, irregular chromatoidal rod, and several bacteria-filled food vacuoles. Chromatin clump of nucleus in face view; 9 by 22 microns. (13) Large, mononucleate cyst with glycogen vacuole, numerous food vacuoles, and chromatin clump in side view; 12 by 13 microns. (14) Binucleate cyst with large glycogen vacuole, large food vacuole, and chromatin clump in face view; 11 by 17 microns.

15 to 23.—Small race of *Endamoeba nana* (6-8 microns), stained with iron hematoxylin, except figures 15 to 17, which were drawn from living specimens;  $\times 2800$  (15, 16, 17). Three successive positions of a small *E. nana*, from stool after saline purge, on warm stage; 8 to 10 microns. (18) Sluggish, binucleate, free ameba with oblique and lateral views of peripheral chromatin clump; 5 by 9 microns. (19) Mononucleate cyst with several food vacuoles and no glycogen vacuole of chromatoidal body; 7 microns. (20) The same with small glycogen vacuole, numerous food vacuoles and no chromatoidal rod; 7 by 8.5 microns. (21) Minute binucleate cyst; 5.5 microns. (22) Ellipsoidal cyst with four nuclei; chromatin clumps in face view, three food vacuoles and an irregular chromatoidal body. 7 by 9 microns. (23) Quadrinucleate cyst with chromatin clumps in side or oblique view; 7 microns.

characterize such cases. The most useful method for this analysis has been found by the authors to be the direct smear stained with Donaldson's iodine-eosin stain, as modified by the authors. It is made as follows: Saturated solution eosine in normal salt solution, 2 parts;

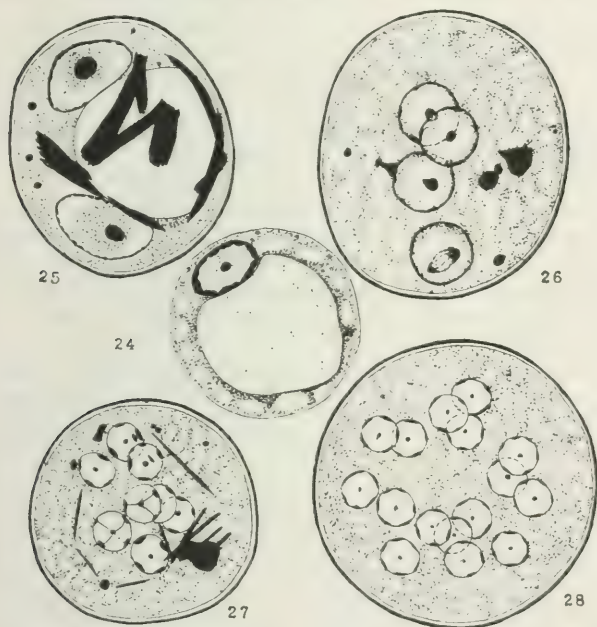


Fig. 5.—24 to 28.—*Endamoeba coli*, stained with iron hematoxylin. 2800. (24) Mononucleate cyst with large glycogen vacuole; 12.5 microns. (25) Binucleate cyst; 15 by 17 microns. (26) Quadrinucleate cyst with irregular, deeply stained masses in the cytoplasm. Nuclei apparently in mitosis; 18 by 20 microns. (27) Cyst with eight nuclei, chromatoidal splinters, and deeply stained masses; 15 microns. (28) Cyst with sixteen nuclei. No chromatoidal splinters; 19 microns.

5 per cent. potassium iodide in normal salt solution saturated with iodine, 1 part; normal salt solution, 2 parts.

The smear is prepared for microscopic examination by rubbing out a minute bit of the feces by rolling it on a round applicator stick in a small drop of normal salt solution and then in an adjacent drop of iodine-eosin

stain. A single cover is placed on both drops and the smear is ready for immediate examination. Living flagellates and unstained cysts appear in the unstained part. In the stained area the bacteria, fecal particles and the intestinal yeasts (except the larger forms) stain at once. Against the pink background the protozoan cysts stand out clearly as bright spherules which soon become tinged with the iodine to varying tones of yellow, while their glycogen-filled vacuoles, when present, turn light or dark brown, according to their mass. The nuclei become more clearly defined as the iodine penetrates, especially in *E. coli*, and *E. dysenteriae*. They are detected with difficulty in this stain in *E. nana*.

Reference is made to concentration methods used by the authors in this work, but they are not recommended for routine examination. A chart indicating the diagnostic features of the three types of entameba mentioned above is presented, and is considered worth reproducing entirely at this place.

Infections of *E. coli* are usually readily distinguished at once in iodine-eosin by size, color and granulations of the cytoplasm, as well as by the prevalent eight nucleate cysts. Individuals are relatively rare in most infections by this ameba.

Infections by *E. nana* are distinguished by the abundance of cysts, the large, clearly defined glycogen mass when present, the prevalence of ellipsoidal or ovoidal cysts, the abundance of highly refractive granules, and, preferably in stained material, the absence of central granule and the clumping of the chromatin on the nuclear membrane in a single blob.

In infections by *E. dysenteriae* the cysts are generally less abundant than in those by *E. nana*, and are distinguished by their glassy, refractive, irregularly vacuolated or (in small cysts) almost homogeneous cytoplasm, with distinct nuclei, central granule and heavy rim, never exceeding four in number, with relatively abundant mononucleates and glycogen, when present, diffusely distributed.

DIAGNOSTIC FEATURES OF *ENDAMOEBIA* DYSENTERIAE, *E. NANA* AND *E. COLI*

Criterion	<i>E. dysenteriae</i>	<i>E. nana</i>	<i>E. coli</i>
Size	(5) 6-15 (20) microns	(3) 5-12 (16) microns	(11) 14-22 (35) microns
Shape	Spheroidal, sometimes asymmetrically rounded	Ellipsoidal in smaller forms, ovoidal in larger; frequently irregular, sometimes spherical	Spheroidal, sometimes ellipsoidal, ovoidal or irregular
Optical properties, unstained	Most highly refractive, glassy, often irregularly vacuolated; light grayish blue; nuclei rarely visible; glycogen mass not visible	Less highly refractive but with highly refractive granules, grayish blue; nuclei invisible; glycogen mass distinct	Least highly refractive, homogeneous, porcellaneous, grayish blue; nuclei faintly visible; glycogen mass faintly visible
Stained with iodine-eosin	Cytoplasm bright greenish yellow; coarsely vacuolated, in small races evenly but finely granular Nuclei distinct with highly refractive, thick border and distinct central granule Glycogen diffuse; if massed, with vague limits	Cytoplasm greenish yellow with numerous small refractive vacuoles Nuclei indistinct, with thin border and peripheral chromatin blob Glycogen dense, in one or more large sharply defined masses, seldom central	Cytoplasm coarsely uniformly granular; yellowish brown Nuclei very distinct with thin granular borders and central granule Glycogen central with vague borders
Nuclei number	Cyst stains red more quickly 1-30-45% 2-10-30% 3-rare 4-25-55%	Cyst resists stain longer 1-Very common 2-Less common 3-Common in small race, very rare in large one	Cyst usually resists stain longer 1-Very rare 2-Rare 3-Very rare 4-Very common 5-Very common 6-Very common 7-Very common 8-Very common 9-Very common 10-Very common 11-Very common 12-Very common 13-Very common 14-Very common 15-Very common 16-Very rare
Structure	Central granule distinct; peripheral chromatin distributed rather evenly in small plaques	No central granule; nuclear membrane indistinct; peripheral chromatin gathered in a single blob on the membrane	Central granule distinct, peripheral chromatin in a few large plaques on the nuclear membrane
Chromatoid substance	In one stout bar or several slender bars with rounded ends. Present in about 50% of the cysts	In several rounded or irregular masses. Rarely present	In stout or slender columns with square or sharp ends. Present in about 5-10% of the cysts
Cyst wall	Thin, distinct	Variable, less distinct	Thicker, very distinct
Size races	Very evident. Small race at 7 microns, large race at 13-14 microns, and one at 10 microns are the most frequent	Very evident. One at 5-7 microns, and one at 8-10 microns, and probably a still larger one at 12-15 microns, most frequent	Less evident. Probably one at 15, one at 18 microns and one larger



## YELLOW FEVER

**Clinical Features and Pathologic Changes in Yellow Fever.** This is the first of a series of articles dealing with yellow fever, published by H. Noguchi.<sup>5</sup>

In this article the author describes the clinical features and pathologic changes observed in yellow-fever patients admitted to the yellow-fever hospital at Guayaquil. He states at the outset that in an analysis of 172 cases, no clinical or pathologic facts were brought to light which had not been described by previous students of yellow fever in Guayaquil or elsewhere.

This work was done by the Yellow Fever Commission of the International Health Board, which was composed of Dr. Arthur I. Kendall, Dr. Charles A. Elliott and Mr. Herman Edward Rodenbaugh of Northwestern University Medical School of Chicago; Dr. Mario Lebrede of Las Animas Hospital, Havana, Cuba, and Dr. Hideyo Noguchi of The Rockefeller Institute for Medical Research, New York.

**Transmission of Yellow Fever.** The second article in this series by Noguchi<sup>6</sup> has to do with the transmission experiments on yellow fever. In summarizing his work Noguchi says that by injecting into guinea-pigs the blood from yellow-fever cases occurring in Guayaquil, a group of symptoms and lesions closely resembling those observed in human yellow fever were induced in a limited number of instances. Of seventy-four guinea-pigs inoculated with specimens of blood from twenty-seven cases of yellow fever, eight, representing six cases, came down with the symptoms, namely, a marked rise of temperature after a period of incubation averaging from three to six days, with simultaneous suffusion of the capillaries, particularly of the conjunctivae and soles, then preliminary hyperleukocytosis followed by progressive leukopenia, the early appearance of albumin and casts in the urine, which gradually diminished in volume as the disease progressed. The fever lasts only a few days, rapidly dropping first to the normal and then usually to subnormal. At this period jaundice mani-

---

(5) Jour. Exp. Med., June, 1919.

(6) Ibid.

festes itself in varying degrees of intensity first in the sclerae then in the skin and the urine. Hemorrhages from the nasal or gingival mucosa or anus have been observed to occur during this period.

Autopsies reveal deep jaundice throughout the entire tissue. The liver is fatty and yellow, the kidney hyperemic, and often swollen and hemorrhagic. Hemorrhagic spots were almost always found in the lungs and gastrointestinal mucosa.

Guinea-pigs are usually rather sensitive to the infection, though many appeared to be somewhat resistant and some even refractory.

The injection of blood of yellow fever patients into ringtail monkeys, rabbits, cats, weasels, and sloths among the mammals, and pigeons, ground-doves, blue-birds, mantas, blackbirds, parakeets, reed-birds, blancos and toucans among the birds, gave negative results.

In the blood, liver and kidneys of the guinea-pigs experimentally infected with the blood of yellow-fever patients, a minute organism was demonstrated which closely resembles in morphology the causative agent of infectious jaundice (*Leptospira icterohaemorrhagiae*).

The leptospira transmitted from yellow-fever cases to guinea-pigs was found to induce similar symptoms and lesions upon further passages into normal guinea-pigs.

The leptospira obtained from cases of yellow fever has been given the provisional name of *Leptospira icteroides*.

**Symptomatology and Pathology.** This is the third article dealing with yellow fever, published by Noguchi.<sup>7</sup>

Under the heading of "mode of experimental infection," Noguchi states that infection with this organism may be induced either by injection into the peritoneal cavity, the blood circulation, or the subcutaneous tissues, or by application to the scarified, depilated surface of the skin or to the mucous membrane, or by feeding the animal with infected tissue or culture.

This report includes the results of study on the types of disease produced in guinea-pigs, dogs and monkeys by inoculating them with the blood or organ emulsions of guinea-pigs or other susceptible animals experiment-

---

(7) Jour. Exp. Med., June, 1919.

ally infected with *Leptospira icteroides*, and also with a pure culture of the organism.

Particular attention has been given in these experiments to the clinical features of the experimental infection in the various animals and to the pathologic changes resulting from the infection.

The symptoms and pathologic lesions induced in guinea-pigs are much more pronounced than those observed in dogs or marmosets. The period of incubation is nearly the same in all three species, from seventy-two to ninety-six hours with intraperitoneal or subcutaneous inoculation, and a day or more longer when the infection is induced percutaneously or *per os*. The febrile reaction in the guinea-pig and marmoset is about the same; in the dog there is less fever. The amount of albumin casts, and bile pigments in the urine is more abundant in the guinea-pig and marmoset than in the dog, and these animals also appear on the whole to become more intensely icteric. The black or bilious vomit, however, though occurring frequently in dogs during life, is observed in the guinea-pig and marmoset at autopsy. The hemorrhagic diathesis is most pronounced in guinea-pigs, less so in marmosets, and least in dogs. In dogs, for example, subcutaneous hemorrhages almost never occur, and the lungs usually show only a few minute ecchymoses. The pleurae, pericardium, and other serous surfaces of the thorax and abdomen remain free from ecchymoses, which, however, with hyperemia, are very marked along the gastro-intestinal tract.

The symptoms and lesions observed in animals experimentally infected with *Leptospira icteroides* closely parallel those of human yellow fever.

The pathologic changes occurring in human cases of yellow fever are similar to those induced by inoculation in guinea-pigs and marmosets and in respect to their intensity stand intermediate between those arising in the two animals mentioned.

**Acquired Immunity to Yellow Fever.** The fourth installment of study on the etiology of yellow fever by H. Noguchi,<sup>5</sup> deals with the acquired immunity of guinea-pigs against *Leptospira icteroides* after the

(8) Jour. Exp. Med., July, 1919.

inoculation of blood from yellow-fever patients. While the majority of guinea-pigs inoculated with blood from these patients escaped a fatal infection, there were a number of instances in which the inoculation induced in these animals a temporary febrile reaction, on the fourth or fifth day, followed in some cases by a slight jaundice, but with a rapid return to normal. Most of these guinea-pigs when later inoculated with an organ emulsion of a passage strain of *Leptospira icteroides* resisted the infection. On the other hand, the animals which had previously been inoculated with the blood of malaria patients or normal guinea-pigs died of the typical experimental infection with the infectious organ emulsion.

It appears from the results that a number of non-fatal, mild, or abortive infections follow the inoculation of blood of yellow-fever patients into guinea-pigs. The fact that such animals were refractory to a subsequent attempt to infect with a highly virulent passage strain of *Leptospira icteroides* is an indication, judging from the reciprocal immunity reaction, that they actually passed through an infection with the same organism, or a strain closely related to it, as that which was used for the second infection experiment.

**Relation of Blood Serum of Yellow Fever Patients to the Infecting Organism.** In this article,<sup>9</sup> the serum from a number of persons recovering from yellow fever in Guayaquil was studied with a view to establishing its possible immunologic relationship with a strain of *Leptospira icteroides* derived from one of the yellow-fever patients. For this purpose, the serum of convalescents was mixed either with an organ emulsion of a passage strain, or with a culture of the organisms, and inoculated intraperitoneally into guinea-pigs.

The Pfeiffer reaction was first studied, and then the animals were allowed to live until the controls, inoculated with the same emulsion or culture of *Leptospira icteroides*, but without the serum, or with serum from patients suffering from other diseases than yellow fever, had died of the experimental infection with typical symptoms. A positive Pfeiffer phenomenon was observed in fifteen of the eighteen convalescent cases

(9) Noguchi: Jour. Exp. Med., July, 1919.

studied, or approximately 83 per cent. Serum from ten non-immune soldiers and from two malaria patients gave uniformly negative results. Protection from an ultimate fatal infection was afforded some of the guinea-pigs which received the serum of yellow-fever convalescents, while the control animals succumbed to the infection with typical symptoms. In one instance in which the serum was tested on the second and tenth days of the disease, a Pfeiffer reaction was demonstrated, as well as protective property against the infection in the specimen from the tenth but not in that from the second day.

From the foregoing observations of immunity reactions it appears highly probable that *Leptospira icteroides* is etiologically related to yellow fever.

**The *Leptospira Icteroides*.** This article by Noguchi is devoted to the cultivation, morphology, virulence, and biologic properties of *Leptospira icteroides*.

As the nature of the causative agent of yellow fever was unknown, the author considered it necessary at the beginning of these experiments to formulate a special method of cultivation. The methods employed were similar to those recommended for the cultivation of *Leptospira icterohemorrhagiae* (Inada and Ido). The principal medium consisted of one part of serum and three parts of Ringer solution used in a combination of the liquid form and a form made semisolid by adding melted neutral agar (0.3 per cent.) the liquid half (8 c.c.) of the medium being superimposed on the semisolid half (8 c.c.) in a tall culture tube such as that used in the cultivation of spirochetes, by the same author.

The results of this particular phase of the work as in each of the other articles are summarized, and this summary is here used entirely. No credit is claimed for abstracting these articles, as the material is very concisely and compactly put in summaries at the end of each of them.

In this instance Noguchi says that by the employment of methods designed to promote the growth both of aërobic and anaërobic organisms, particularly those belonging to the class of spirochetes, it was possible to



obtain a pure culture of a delicate organism, the morphologic features of which place it in the genus *Leptospira*. On three occasions, that is, from three out of eleven cases of yellow fever, the organism was directly cultivated. These three strains were found to induce the characteristic symptoms and lesions when tested on guinea-pigs. The organism was designated *Leptospira icteroides*.

*Leptospira icteroides* was also obtained in pure culture from the blood of guinea-pigs which succumbed to infection after being inoculated with the blood or organ emulsions from patients suffering from yellow fever. These cultures also proved to be virulent when tested on susceptible animals.

The morphologic characteristics and certain biologic properties of the organism were considered in detail. It is invisible under translucent illumination and is difficult to stain by most aniline dyes. It is highly sensitive to the presence of bacteria and is rapidly destroyed in a medium in which certain other organisms are present. The presence of blood serum (man, sheep, horse, rabbit, etc.) seems to be essential for its growth. It grows well at a temperature of about 25-26° C., and more quickly at 37° C., though at the latter temperature it dies out within a few weeks. At 25° C. under favorable conditions and in suitable culture media it remains viable for several months without losing its virulence. *Leptospira icteroides* multiplies by transverse division.

The virulence attained by some strains was such that 0.00001 c.c. of a culture could induce typical fatal infection in guinea-pigs. There exists a considerable variation among guinea-pigs in their susceptibility to *Leptospira icteroides*.

The organism is killed within ten minutes at a temperature of 55° C. and is also destroyed by complete desiccation or freezing and thawing. Bile and bile salts dissolve it in certain concentrations, but not sapoin.

*Leptospira icteroides* passes through the pores of Berkefeld filters V and N, and there is a possibility that it has a granular phase of life under certain conditions.

**Leptospira Icteroides in Blood and Urine of Yellow-Fever Patients.** This article by Noguchi<sup>2</sup> deals with the demonstration of *Leptospira icteroides* in the blood tissues and urine of yellow-fever patients and of animals experimentally infected with the organism. Examination of fresh blood from yellow-fever patients by means of the dark-field microscope, made in more than twenty-seven patients revealed in three cases the presence of *Leptospira icteroides*. In no instance was a large number of organisms found, a long search being required before one was encountered. The injection of the blood into guinea-pigs from two of the three positive cases induced in the animals a fatal infection, while the blood from the third positive case failed to infect the guinea-pigs fatally. Careful but by no means exhaustive dark-field searches for the leptospira with fresh specimens of blood from the remaining cases of yellow fever ended without positive findings, although four of the specimens, when injected into guinea-pigs, caused a fatal leptospira infection.

Regarding the presence of *Leptospira icteroides* in various organs, both dark-field and stained films were examined. In only one instance were a few organisms detected in the emulsion of liver taken shortly after death from a person dying on the fourth day from yellow fever.

In experimental infection of guinea-pigs with *Leptospira icteroides* the blood became infective in many instances forty-eight hours after inoculation, and was always infective after seventy-two hours. The liver and kidney become infective simultaneously with the blood. Detection of the organism by means of the dark-field microscope has seldom been accomplished before the fifth day.

**Search for Organism of Yellow Fever in Wild Animals.** The next step in this work by Noguchi<sup>3</sup> on yellow fever consisted of determining whether or not leptospira could be found in wild animals in Guayaquil and the relation of these organisms to *Leptospira icterohaemorrhagiae* and *Leptospira icteroides*. The question

---

(2) Jour. Exp. Med., August, 1919.

(3) Ibid.

of the presence of a leptospira in tropical countries, especially where endemic foci of yellow fever exist, has not heretofore been studied, but with the isolation of a pathogenic leptospira from certain cases of yellow fever in Guayaquil the relation between the human and animal strains was considered to demand a thorough investigation. A general survey was made to detect the presence of leptospira among the wild animals encountered in Guayaquil.

It is concluded from the work conducted along these lines that the leptospira isolated from the kidneys of wild rats and mice in Guayaquil belongs to the group of *Leptospira icterohaemorrhagiae* and differs from *Leptospira icteroides* in its immunity reaction.

**Mosquitoes in Relation to Yellow Fever.** In order to carry out this investigation, Noguchit collected larvae of *Stegomyia calopus* from houses in Guayaquil, and kept the imagos which emerged from the larvae in special cases. Attempts were made to reproduce the appearances of yellow fever in the guinea-pig by permitting these mosquitoes to bite the animals after having fed upon the blood of yellow-fever patients during the early stage of the disease.

From these experiments the author says that it appears that even under natural circumstances the percentage of mosquitoes that eventually become infected with yellow fever microbes by sucking the blood may be very small. Apparently a mosquito occasionally becomes infected by taking up the one or two organisms which happen to be circulating in the peripheral blood of man, and it is these occasionally infected few which carry the disease. It is not difficult to realize the extent of ever-increasing danger from a constant supply of the microbe virus which an endemic center or an epidemic of yellow fever can provide. One infected mosquito may mean many patients and the life of such a mosquito is usually longer than that of the person whom it fatally infects.

Finally, it is of interest to note that the development and maintenance of *Leptospira icteroides* are indispensably associated with the blood constituent, the

(4) Jour. Exp. Med., October, 1919.

serum, and this is amply supplied by the blood-sucking insect. The organism is one of the most fragile of all the pathogenic parasites and can not survive the concurrence of other less fastidious organisms such as bacteria. The comparatively aseptic body cavity of the *stegomyia* furnishes a secure shelter for the parasite, which undoubtedly penetrates the zone of safety as soon as it is taken into the stomach of the insect. Unlike many other parasites, this organism is capable of penetrating the intact skin or a bacteria-proof filter, and hence it is probably an easy matter for it to pierce the tissue of the visceral organs of the mosquito. Whether or not *Leptospira icteroides* can survive and multiply only in the body of *Stegomyia calopus* and not in other varieties or genera is yet to be determined.

Another interesting fact with regard to the extrinsic life of this organism is that it can multiply steadily at a temperature of from 18 to 37° C. The optimum temperature, at which it remains viable for many months, is 28° C. The climate in most of the tropical countries offers optimum conditions both for *Leptospira icteroides* and for the mosquito which carries and nourishes it.

## SAND-FLY FEVER

### **Sand-Fly Fever and Its Relationship to Dengue.**

While the subject of sand-fly fever and its relationship to dengue may not interest materially many physicians in the United States, they are diseases that have to be reckoned with and a brief record of work being done on them is not out of place here.

The conclusions reached by J. W. D. Megaw,<sup>1</sup> after a thorough study of this subject are as follows:

Though at first sight it almost appears obvious that dengue and sand-fly fevers are quite distinct from each other, the evidence when analyzed is by no means convincing. Until some reliable point of distinction between them is discovered, it is better to stick to the old term "dengue."

The terms three-day and seven-day may be added, if desired, to show the duration of the disease in any

---

(1) Indian Med. Gaz., July, 1919.

particular case, but they are not suitable as titles for the disease.

Even if the balance of opinion should be in favor of regarding sand-fly fever as being distinct from dengue, there can be no justification for giving a long separate account of the two diseases. The utmost that can possibly be said by way of description of sand-fly fever is something like this: "It is a disease which is either one of the modifications of dengue or is closely related to dengue. Those who consider it to be different from dengue say that it can be distinguished by the absence of a rash and by the absence of a secondary rise of temperature, though it must be admitted that in many outbreaks of undoubted dengue numbers of cases show neither rash nor secondary fever. There is also a possibility that dengue is conveyed by a mosquito, while sand-fly is conveyed by a "*Phlebotomus*."

If this is the utmost that can be argued by the "dualists," and if they will confine themselves to the above line of action, no quarrel can be had with them. It is when they complicate the text-books and confuse students and practitioners by long and unnecessary descriptions that it is essential, says Megaw, to issue a definite challenge to them.

## TRENCH FEVER

**Spirochetes in the Blood in Trench Fever.** In trying to determine the cause of trench fever, A. C. Coles<sup>2</sup> examined films of blood, air dried, from successfully inoculated or scarified men who developed trench fever. In two out of six of these cases, he found a few spirochetes or spirochete-like bodies, in one or two of the many blood films examined. These spirochetes or spirochete-like structures varied considerably in their forms, but they had in common the fact that they all stained with Giemsa a delicate blue tint. They were all faintly granular and in no case were the ends pointed.

The questions which naturally arise concerning these findings are, whether or not these were actual spirochetes, and if so, what relation did they have to trench fever?

<sup>(2)</sup> Lancet, March 8, 1919.



They had the general appearance of spirochetes, although those from the second patient were very elusive, of slight refractive power and very difficult to see. The staining reactions with Giemsa, a pale blue color, are not, however, common in spirochetes in general. They cannot be regarded as artefacts, and the faint irregular structures seen can not be compared to streamers, which in the author's experience are never encountered in ordinary air-dried, stained films. Whether these bodies have any actual causal relation to trench fever, is much more difficult to say. The fact that they were detected only in the blood of definite cases of artificially induced trench fever, and then only during the first attack of fever, is at least suggestive. The generally accepted statements that at least in one stage of development, the virus of trench fever is filterable, does not exclude that virus being a spirochete. Some spirochetes are known to be filterable and Noguchi states that the *Spirochæta icterohaemorrhagiae* will pass the Berkefeld V.

## MEASLES

**Insusceptibility of Man to Inoculation with Blood from Measles Patients.** An attempt to produce measles in human subjects by inoculating them with blood and with secretions from subjects who suffered from acute measles has been made by A. W. Sellards,<sup>4</sup> of the Medical Corps, U. S. Army. This is a long and complete article and any attempt to present the results in a few lines would be entirely devoid of most of the value to be gained by this work. Therefore, the author's methods and discussions are used extensively, and, it is considered, to great advantage.

The first inoculations were designed to give preliminary information on the following points:

1. Whether the serum alone, free from red cells, contains the virus of measles.
2. Whether the organism of measles will pass through a Berkefeld filter.

---

(4) Bull. Johns Hopkins Hosp., September, 1919.

3. Whether a series of injections of patient's and convalescent's serum would immunize a human subject without producing an attack of the disease.

4. Whether a previous attack of measles confers complete immunity or whether a modified attack might result in a partially immune subject with possible attenuation of the virus.

For these inoculations, blood was taken from a moderately severe case of measles twelve hours after the first appearance of the rash. At this time, the Koplik spots had already disappeared, the eruption was profuse over the face, back and chest, less intense over the abdomen and only a few scattered spots had appeared on the thighs.

Blood taken from measles patients was so treated that by inoculating four susceptible volunteers the above-mentioned four points were determined. None of the four individuals developed any symptoms of measles.

The next step in this work consisted of inoculation of defibrinated blood and of blood incubated in ascitic broth. The remainder of the work with susceptible individuals was restricted to an attempt to transmit measles by the injection of the patient's blood. Defibrinated blood was injected subcutaneously in two men. Cultures of patient's blood in ascitic broth were inoculated in two other men. This duplication of the method for which successful results have been reported seemed essential in view of the negative results following the inoculation of serum without preliminary incubation. None of these four subjects developed measles, neither did any symptoms appear that could be definitely attributed to the injection.

After an interval of thirty-five days, one of the men injected with defibrinated blood and another injected with blood incubated in broth were re-inoculated by smearing the mucous membrane of the eyes, nose and throat with freshly excised morbillous skin lesions. These inoculations possessed a two-fold interest, in that a positive result would demonstrate that the virus of the disease is present in the skin lesion and that these individuals who were refractory to an injection of the blood were, nevertheless, susceptible to the disease. No definite symptoms developed.

The next step in the process consisted in inoculating two susceptibles on two successive days with blood taken before and after the appearance of the eruptions. No symptoms of measles were produced in any of the four volunteers so subjected.

When it became apparent that no symptoms of measles would develop from these injections of blood, arrangements were made to test the susceptibility of these men by inoculating the mucous membranes of the eyes, nose and throat with a secretion from the mucous membrane of an early stage of measles.

In a *résumé* the author states that an effort has been made to determine whether the virus of measles exists in the circulating blood of the patient permitting the transfer of the disease from man to man by the inoculation of blood. The prominent data bearing directly on this subject are:

1. The successful transmission in two cases previously reported by Hektoen.

2. The failure in eight instances recorded in this paper to transmit measles by the injection of blood.

3. The clinical phenomenon of the origin of the rash on the face or upper part of the body with its gradual progress downward requiring from one to three days to complete this march.

The symptoms of the two experimental cases that have been reported were not entirely characteristic of the classical type of measles. Although the disease varies extremely little in its clinical manifestations, distinct modifications might readily occur under experimental conditions.

As regards the negative results obtained in these eight individuals, the principal difficulty arises in establishing, by the clinical history, the susceptibility of an adult to a disease so generally prevalent as measles. In some of the men who were inoculated the circumstantial evidence of susceptibility was unusually strong.

Failure to transmit the disease by the injection of blood does not preclude the existence of the virus in the blood stream even in moderate amount. There is some evidence that these men not only failed to become infected but that they were actively immunized by the

injection of blood; such an assumption would, of course, presuppose the existence of the virus in the blood stream. Indeed the agent which excites the rash might readily gain access at least temporarily to the blood-stream regardless of whether its distribution takes place by the lymphatics or by the circulating blood.

The constant origin of the eruption on the upper part of the body and its gradual and orderly extension downward is quite unlike the development of eruptions in which the virus is known to be distributed by the circulating blood.

Measles originates as an infection of the respiratory and conjunctival mucous membranes and the virus does not set up metastatic infections in the viscera of the body in the spontaneous disease. Failure to reproduce the disease by subcutaneous injection of the virus is in keeping with the behavior of several other pathogenic microorganisms of the respiratory and gastro-intestinal tract.

The virus of measles *per se* does not produce serious effects, but one attack of the disease gives rise to a well-marked immunity. With appropriate isolation of the virus it would seem that a substantial active immunity should be obtainable with a minimum of inconvenience to the individual.

In conclusion, Sellards considers that the question of the transfer of measles from man to man by the injection of a patient's blood is entirely reopened by the eight successive negative inoculations recorded in this paper.

The failure to transmit the disease in this manner does not necessarily exclude the possibility of the occurrence of the virus of the disease in the circulatory blood; some evidence was obtained indicating the possibility of producing active immunity by the injection of patient's blood.

**The Occurrence of the Pfeiffer Bacillus in Measles.** During the autumn of 1918, when influenza and measles were prevalent, certain similarities between the two diseases were noticed by A. W. Sellards and E. Sturm,<sup>5</sup> who record their observations in this article.

With the onset of influenza at Camp Devens, Mass.,

---

(5) Bull. Johns Hopkins Hosp. November, 1919.

where these observations were made, the symptoms in the earlier cases were distinctly less fulminating than at the height of the epidemic. The possibility of measles in the pre-eruptive stage required consideration in establishing the diagnosis of the first group of influenza patients admitted to the base hospital. The acute onset of conjunctival and respiratory symptoms was accompanied with a pronounced leukopenia. Other noteworthy similarities between the diseases were also noted. Both are highly contagious and are frequently complicated by pneumonia in its various forms. The occurrence of the Pfeiffer bacillus in a high proportion of cases has been reported in measles as well as in influenza. At the time of this epidemic the authors were engaged in a study of measles, and considered it advisable to investigate the occurrence of Pfeiffer and Pfeiffer-like organisms in measles patients.

There follow a summary of the literature dealing with this subject, and also a detailed account of the study and experimental work done by the authors on this problem. From the results obtained they conclude and state that the examination of a group of measles cases occurring a few weeks after an epidemic of influenza showed the presence of an organism indistinguishable from the Pfeiffer bacillus in twenty-five out of thirty-one cases.

This organism was obtained readily from the sputum and with little difficulty from the conjunctivae. A highly parasitic, hemoglobin-requiring organism was obtained in one or two cases from an excised inguinal gland. The Pfeiffer organism was not obtained from the blood stream nor from the excised skin lesion.

With the subsidence of the active symptoms of measles these microorganisms disappeared rather rapidly in about three-fourths of the cases.

Cultures of the Pfeiffer organism from cases of measles failed to colonize when inoculated on the mucous membrane of four healthy volunteers, two of these individuals supposedly had not had either measles or influenza.

A comparison was made of the strains of the Pfeiffer bacillus isolated from measles and from influenza. The results showed considerable variation in the behavior of



the individual strains. It is theoretically possible that the hemoglobin-requiring bacilli represent a group of microorganisms containing distinct species.

The occurrence of the Pfeiffer bacillus in measles and in influenza constitutes suggestive evidence against its etiologic relationship in either disease. This evidence would be materially strengthened provided the identity of the strains from these two sources were accurately established.

The evidence which is available at present is not sufficiently complete to exclude the specific etiologic rôle of the Pfeiffer bacillus in some of the acute respiratory diseases.

**Concerning the Etiology of Measles.** This attempt at determining the etiology of measles was made by A. W. Sellards and A. Wentworth.<sup>6</sup>

Measles though usually a mild disease in itself, often it leads to serious consequences. Its involvement of the upper respiratory tract frequently facilitates the invasion of the lungs by a hemolytic streptococcus or the pneumococcus. The resulting pneumonia has attracted considerable attention of late. Control of the hemolytic streptococcus infections by specific vaccines or serum therapy is a difficult problem. A possible departure from this line of approach consists in the prevention of measles itself by the development of a prophylactic inoculation. The clinical features of the disease indicate the existence of an excellent theoretical basis for the development of a protective inoculation. One attack of measles confers a high degree of immunity, and the virulence of the causative organism is naturally so low that, *per se*, it does not produce fatal effects in man under ordinary conditions. The crucial problem is whether the virus of measles can be still further attenuated in such a manner that it would be suitable for prophylactic purposes.

There follows a review of the literature that has accumulated by various authors in attempting to find the organism that produces measles. Experimental work carried out by the present authors consisted in inoculating monkeys, (*M. rhesus*), from cases of measles occur-

(6) Bull. Johns Hopkins Hosp., March, 1919.

ring in adults of from 20 to 30 years of age. Blood was the only material used for inoculating and in all cases it was withdrawn within the first twenty-four hours after the appearance of the rash. It was either defibrinated or collected in sodium citrate solution prepared in physiologic saline. Observations on the inoculated animals were made each day about the middle of the forenoon, especial attention being given to the body temperature and the leukocyte count. The animals were extremely well kept and accessory influences were well guarded against.

In order to test out any doubtful symptoms occurring in the inoculated monkeys, arrangements were made to inject blood from them into susceptible human volunteers. Strict precautions were taken to select human volunteers who had not had an attack of measles, and who did not harbor pathogenic organisms in the respiratory passages.

Three animals were inoculated intraperitoneally each from a different case of measles. The animals remained entirely free from any symptoms that either were diagnostic or even suggestive of measles. Two of these animals that were injected a second time failed to develop any symptoms.

After an incubation period of eleven days blood was taken from one of these monkeys and injected into a human volunteer. No symptoms developed.

## MUMPS

**The Cerebral Complications of Mumps.** A discussion of cerebral complication of mumps, with a report of nine cases, is made by R. L. Haden.<sup>8</sup> The reader is reminded that at times there are other complications than orchitis in patients who suffer from mumps, and that these complications make the course of the disease a severe one. Death, when resulting directly from mumps, Haden says, is probably always due to cerebral complications.

Approximately 150 instances of cerebral complications of mumps, exhibiting quite a variety of symptoms,

(8) *Archiv. Int. Med.*, June, 1919.

have been reported. Many factors point to the fact that the fundamental condition in these complications of mumps is an encephalitis and not simply a meningitis. In most cases the cerebral symptoms are out of all proportion to the meningeal reaction, as is evidenced by the pathologic findings in the spinal fluid. The common symptoms are high fever, headache, nausea and vomiting. Usually there is only slight rigidity of the neck, and not a well-marked Kernig's sign. Numerous instances occur of undoubted involvement of the cerebrum alone. In these there are no definite meningeal signs and no pathologic findings in the spinal fluid. Among the symptoms noted in thirty-one patients, reported by Acker, were unilateral convulsions, monoplegia, hemiplegia, aphasia, speech disturbances, psychoses, disturbances of sensation and stupor. Such symptoms point to a true involvement of the brain substance. The other predominant symptoms, such as bradycardia, headache, vomiting and optic neuritis are thought to be probably the direct results of intracranial pressure.

Nine patients suffering from mumps, complicated with cerebral involvement, were observed in the base hospital at Camp Lee by Haden. During the time covered by this report, 476 patients with mumps were admitted to the hospital. Usually, as the parotitis was subsiding, there was a marked rise in temperature, with little change in pulse rate, severe headache, nausea, and vomiting, and often the patient had an orchitis. On examination the patient was dull, answered questions slowly, showed slight stiffness of the neck, a suggestive Kernig's sign, and variable reflexes. Lumbar puncture gave a clear fluid with a lymphocytosis, and was under increased pressure. It is the author's opinion that the number recorded in this series of patients does not indicate the true percentage of cerebral involvement. Often patients were observed with severe headache and fever, sometimes with vomiting, occurring in the course of mumps. There were no other signs of meningitis and nothing was found elsewhere to account for the symptoms. During the studies of these patients little doubt was entertained as to the nature of the infection. Smears and cultures were made from the spinal fluid of each

patient and Gram-positive cocci were found in smears from the fluid in one instance. Lumbar puncture was found to be an effectual therapeutic agent. The temperature usually fell to normal quickly, and the headache was relieved following the withdrawal of spinal fluid.

In the original article there appear detailed descriptions of these nine patients, including history, a description of the clinical course and laboratory findings.

**Mumps in U. S. Navy Hospital.** This article is based on a study of 120 cases of mumps. The interest of the authors, R. B. H. Gradwohl, C. F. Carter, and H. L. Fougereuse,<sup>9</sup> displayed itself in the following manner: An attempt to isolate an organism from the blood of these patients, a study of the cases with a view of tabulating the prominent symptoms, a study of the blood picture in all cases, a notation of the complications of the disease, and an effort to apply specific medication in the shape of a convalescent serum.

The last of these points mentioned is the one that attracts the most attention. Blood was drawn from convalescent patients in the usual manner and the usual routine tests were made. The serum was injected subcutaneously for the greater part. Very little reaction was noted in the subcutaneous injections. When intravenous injections were made there were more symptoms, some patients developing severe chills and high fever.

The authors were particularly struck by the remarkable effects of these injections on the complications of mumps, to wit, a lessening of pain and earlier subsidence of swelling, together with an earlier drop in temperature. In one case, with localized pain in the region of the pancreas, extreme discomfort and a very high temperature, the administration of 5 c.c. of convalescent serum was followed within two hours by a marked drop in the temperature and abatement of pain. In this instance, opiates had been administered, local applications, etc., had been used before using the serum, and no success had been obtained by these measures. In a parallel case, with extreme pain in the testes from orchitis, relief was obtained within five hours. In general, the observations

<sup>9</sup>U. S. Naval Med. Bull., October, 1919.

were that convalescent serum abated the pain and fever very promptly in complicated cases.

Regarding the use of this serum as a prophylactic measure, the authors prepared a large quantity for future epidemics, and felt sure that it would find a very definite place in the prevention of the spread of this disease among susceptible persons.

This statement seems to be justified on the basis of the report of Hess, who gives the following facts: Twenty children were inoculated with the blood of convalescent mumps patients: from 6 to 8 c. c. were used intramuscularly. Blood was taken from patients just recovered from the disease, from patients recovered ten days, and from patients who had the disease several years previously. All these children, none of whom had ever had mumps, were exposed to the disease and none contracted it. Inasmuch as the period of incubation of the disease is about eighteen days, it is possible to protect children against mumps very easily by this measure.

## PERTUSSIS

**Treatment of Whooping Cough.** A note presenting a simple method of applying resorcin solution that has been found very effective in the treatment of whooping cough, is presented by N. Macleod.<sup>1</sup>

In describing the method, he states that for each case a wire-handled throat brush is needed, which should be bent at first suitably for pharyngeal use. When tolerance there is established, it should be further bent to form almost a right angle, about one and a half inches from its point, proximal and distal parts being straight, for laryngeal brushings; this, he says, is quite practicable without artificial light and mirrors. He uses a 2 per cent. solution of resorcin in glycerine and water, 1 and 12 parts respectively.

Immediately before each early application of the brush, it is well to put the patient through a preliminary drill in breathing deeply with the mouth wide open and the tongue well protruded to be persisted in while the brush is introduced quickly once around the walls

(1) *Lancet*, Feb. 15, 1919.



of the pharynx. Mucus should be washed off on withdrawal and the brush kept in a tablespoonful of resorcin, renewed daily, to be ready for the next performance an hour later. The procedure should be repeated regularly during the waking periods. In patients shy of the brushing, it is helpful at the first treatment or two to be satisfied with brush introduction short of the pharynx, so that the tongue contact becomes tolerated sufficiently and the sweet taste of the solution experienced, repeated say three or four times on each occasion. Gradually introduced further, the brush soon reaches the pharynx, when a single turn around its walls will suffice. The attempt to enter the larynx should not be made until brush toleration is established in the pharynx.

This cleansing of the wall of the pharynx and larynx is recommended most highly by Macleod as reducing greatly the symptoms of the disease, and also of shortening the duration.

## SMALLPOX

**Vaccination by Injection.** Administration of small-pox vaccine by subcutaneous injection is described by J. R. Goodall.<sup>3</sup>

Before using this method on men in the army, Dr. Goodall had himself vaccinated by subcutaneous injection. This was done by Dr. George Hume, who had used the method to a small extent previous to this time.

Following this trial, Goodall vaccinated hypodermically approximately 6,000 men and a number of officers and children.

*Method of Preparing Vaccine.* It was impossible to procure vaccine in bulk, so vaccine put up in the small capillary tubes was used in the majority of cases.

These vaccine tubes were first placed in methylated spirit for a few minutes, then withdrawn singly by surgically clean or gloved hands, the excess alcohol was wiped off with sterile absorbent cotton, the ends were broken off, and, lastly, the sterile rubber bulb was fixed to one end of the tube to blow out the vaccine into a

---

(3) Lancet, Aug. 16, 1919.

sterile beaker. The vaccine generally shoots out of the tube into the beaker in the form of a small cylinder.

From one-half to three-quarters of a tube of vaccine was used for each individual. Sufficient sterile water was then added to the vaccine to make each injection equal to one cubic centimeter. In private practice, or where one or two only are to be vaccinated, the vaccine may be prepared as an ordinary hypodermic injection using vaccine instead of a drug.

*Technique.* The technique of injection was as follows: The arm was sterilized with iodine and the vaccine injected diagonally with a fine hypodermic needle and syringe into the subcutaneous tissues. In a few cases by mistake the vaccine was injected intracutaneously.

*After-Effects.* In describing the after-effects Goodall says that the local reaction sets in usually between two and four days, but in a few cases the reaction was considerably delayed. In three children the reaction did not appear until twelve, thirteen and fifteen days respectively. The local reaction is much like that following antityphoid inoculation and just as variable in intensity. About 8 per cent. proved ineffective, showing the slight local reaction, not more than perhaps could have been accounted for by the iodine applied to the skin; in 70 per cent. (approximate only) there was a reaction similar to the usual reaction after antityphoid inoculation—*i. e.*, local swelling, heat, tenderness, slight pain, and redness. In a small percentage of cases the reaction was marked, causing swelling and edema of the elbow, and in a few edema involving the whole arm and hand.

In every one of the 6,000 cases vaccinated hypodermically, either under the supervision or by the author, the local conditions subsided without any signs other than those of excessive local reaction.

After the seventh or tenth day the local swelling and induration subsided, leaving a hard nodule in the subcutaneous tissue, usually ill-defined at first, becoming later well circumscribed and lasting for about one month. This is quite painless after the first acute reaction. The process differs in no respect from that of an antityphoid reaction, except that the onset is slower and the reaction spreads itself over several days. The

general symptoms vary in intensity and do not differ from those of ordinary vaccination.

In the 6,000 cases quoted here there was not one case of infection. This Goodall declares can be stated without question of doubt.

None of the 6,000 required dressings and the men were not exempted from anything but physical training and rifle drill. A percentage were given light duty and a very small percentage were excused duty for a few days, owing to excessive local or general reaction. There were no hospital admissions. In a few cases (about ten altogether) the vaccine was injected intradermically, and about four or five days later there developed the typical vesicular and pustular stages of ordinary vaccination, quite uncomplicated.

*Advantages of the Method.* This is a clean surgical operation. If untoward results develop they are due to faulty technique. There is no open wound, and therefore dressings are not required. Dangers of secondary infection are practically eliminated. The percentage of positive reactions is very high. In only a small percentage of cases the local and general symptoms caused complete incapacity. It is painless as compared with scarification. Children undergo the hypodermic vaccination without any difficulty, owing to the rapidity with which the injection is carried out.

## CHOLERA

**Recent Researches on the Etiology of Cholera.** In discussing this subject, Lieut.-Col. E. D. W. Greig<sup>4</sup> states that at the time he commenced the investigation of cholera, it was generally considered that the cholera vibrio was confined to the alimentary tract of man, but bacteriologic examination of the organs of cholera cases, made shortly after death, have demonstrated that it has a much wider distribution in the tissues. The results of these observations in one case are shown in the following table:

---

(4) Edinburgh Med. Jour., July, 1919.

Organs Examined Bacteriologically	Presence or Absence of Comma Bacillus
1. Left lung .....	+
2. Right Lung .....	+
3. Wall of left ventricle of heart.....	+
4. Liver .....	+
5. Gall bladder—	
(a) Portion of wall.....	+
(b) Bile .....	+
6. Spleen .....	+
7. Pancreas .....	+
8. Left kidney .....	+
9. Right kidney .....	+
10. Lymphatic gland (mesenteric).....	+
11. Urinary bladder—	
(a) Urine .....	+
(b) Portion of wall .....	+
12. Cerebrum .....	+
13. Choroidal plexus .....	+
14. Fluid in right lateral ventricle.....	—
15. Fluid in left lateral ventricle.....	—

In 271 postmortem examinations in which the bile was examined bacteriologically, the vibrio was found to be present in eighty, and in twelve of these definite signs of cholecystitis were noted with the naked eye.

It has been found that bile forms a suitable medium for the growth of the vibrio, and in the gall-bladder there is an absence of inhibiting organisms, such as are present in the intestinal tract. Some organisms found in the intestines are particularly unfavorable to the development of the vibrio, for example, the *B. pyocyaneus*, *B. proteus* and *B. lactis aërogenes*. In chronic carriers, the vibrio lurks in the gall-bladder for long periods, probably for years. During all that time they escape into the intestine and thence into the outer world, where they start fresh infections.

This is clearly demonstrated in epidemics which have been systematically investigated by modern methods of research. It proves how important the carrier is, and how essential is the control of infected individuals. The latter is a very difficult problem to solve.

Results of the examination of stools of a single patient convalescent from cholera are tabulated, and they show that the organism may recur in the feces at intervals of as long as twenty days.

The author has examined the urine bacteriologically in fifty-five cases of cholera, and has been able to cultivate the vibrio eight times. In two of the eight cases, the patients had quite recovered and were fit for work. This observation has, of course, an important bearing on the question of the prevention of cholera.

Bacteriologic examinations of the blood of patients with cholera were negative at all times. It is considered not improbable that the vibrios are carried mainly by the lymph stream.

All the facts considered in this discussion will lead to the conclusion that an essential measure in an intensive anticholera campaign is the detection of the infected person, especially the carrier. This is not an easy matter, but although the difficulties are great, every effort should be made to overcome them by perfecting and rendering more precise the machinery for dealing with the question. It is further essential that all measures should be based on the results of scientific research.

**Treatment of Cholera.** The latest method of treating cholera is presented by M. P. Chacko,<sup>5</sup> who had been lately assigned to special cholera duty at Trivandrum. He merely presents a record of patients treated by the intravenous injection of hypertonic saline as suggested by Sir Leonard Rogers.

Transfusion with hypertonic saline accomplishes something more than reinforcing the blood-pressure. The introduction of calcium chloride arrests the tendency to oozing from the capillaries and arterioles of the intestinal tract, and indirectly aids in arresting the frequent evacuations.

While a blood-pressure of 70 is considered an absolute indication for using this form of treatment, the author thinks that even when the blood pressure is above 90 improvement in the condition of patients may still be expected from infusion.

Concerning the amount of fluid to be given, he says that the symptoms in the recipient that call for cessation of transfusion are rigor, frontal headache, precordial pain, high blood-pressure, and failure to raise the blood-pressure, though fluid is ascertained to be flowing

(5) Indian. Med. Gaz., August, 1919.



in the veins. These symptoms have been observed in only ten of the patients treated by Chacko. He has never noticed injurious distension of the heart from the increased volume of fluid in any of his patients. On an average from 2 to 3 pints may be injected into an adult without producing any symptoms. He considers that the benefits of saline transfusion will vary with the class of case and the continued attention one is able to give the patient at the bedside. In a patient whose pulse can be felt at the wrist and whose evacuations have ceased, the effects are likely to be immediate, striking and permanent.

In a patient who is apparently dying, whose pulse can not be felt at the wrist, whose voice is hoarse, whose limbs are rigid, whose evacuation continues even after the injection, the results are far from satisfactory.

In a patient whose pulse-rate does not diminish in frequency, whose blood-pressure does not improve after the injection, the results are not satisfactory.

Chacko still holds, nevertheless, that if saline infusion can be given repeatedly and continuously, some of the patients who would otherwise die may be saved.

Short detailed records of thirty patients thus treated are presented. More than fifty patients were treated by this method by the author, but only representative cases are considered here. The success of the method in the author's hands was barely 50 per cent., but he emphasizes the fact that he worked under great disadvantages much of the time. Permanganate, atropine and other methods of treatment were tried in almost all of the cases before intravenous infusion was resorted to.

## ANTHRAX

**Treatment of Human Anthrax.** The treatment of human anthrax, with the record of a single patient is presented by J. C. Regan and C. Regan.<sup>6</sup>

The patient was a man 26 years old, who, on November 18, while shaving, accidentally cut himself on the right side of the neck. The wound bled a little, but he paid no attention to it, lathering soap over the cut surface with

<sup>66</sup> Amer. Jour. Med. Sci., June, 1919.

a new shaving brush, which he had just purchased, and which previous to use he had washed and placed in some boiling water.

On the following day, about noon, the man began to feel ill, complaining of headache, backache and generalized pains all over the body. Toward evening of the same day, his neck became rather stiff, especially in the right side, so that it hurt him to turn his head around. This he attributed to a small pustule which had developed in the place in which he cut himself. During the night he experienced a slight chill and felt somewhat feverish. He noticed particularly that his eyes pained him so that it was impossible to read.

On the next day, two days after cutting himself, the swelling of the neck had become more marked and painful to touch, and he felt as if it were exerting an inward pressure, but not sufficiently to interfere with respiration or taking nutrition.

Smears and cultures of materials from this wound aroused suspicions of anthrax bacilli, and 48 c. c. of anthrax serum were injected intramuscularly in the right buttock; 10 c. c. were injected into the indurated tissues immediately around the pustule.

On the following day 30 c. c. of anthrax serum were injected into the right buttock and 10 c. c. into the region of the wound.

Two days later, 12 c. c. of serum were injected into the region of enlarged lymph glands, just below the angle of the jaw on the side injured, and two days following that a third injection of 30 c. c. of serum were given into the buttock.

Ten days after the patient was admitted into the hospital he was discharged apparently cured, and when seen some time later was enjoying good health.

The following points in connection with this patient are particularly emphasized by the authors:

The definite history of the manner in which the disease was contracted—accidental cut during shaving, and the use of an infected shaving brush. The mildness of the attack, despite the situation of the malignant pustule in the neck. The subsidence of the local and constitutional symptoms without incision of the lesion. The ap-

parent benefit from the intramuscular injection of anthrax serum. The definite improvement in the pustule itself following the injection of anthrax serum into the indurated tissues of the neck surrounding the lesion. The local use of serum, which is considered one of the prime essentials for the successful treatment of anthrax. The absence of a blood invasion. The recovery of the anthrax bacillus on several different occasions from the pustule, both by smears and cultures. The absolute proof of its identity as anthrax by its morphology, its cultural characteristics, the effect in producing death on inoculation of cultures into mice and, finally, the recovery of the bacillus in pure culture from the animal. (The morphology of the organism in smears from the pustule is not enough to identify it. Its lack of motility and the fact that it possesses a capsule must be proved to differentiate it from the *Bacillus subtilis* and the bacillus of malignant edema.) The recovery of the organism from the shaving brush of the patient. The similarity of the bacillus in its morphology, cultural characteristics and results upon animal inoculation to that which was found in the malignant pustule.

**The Local Use of Anti-anthrax Serum in Treatment of Anthrax.** Various methods of local treatment have been tried in the therapy of anthrax. Among the measures used to destroy the pustule are excision, the application of chemical or thermal cautery, and the injections of germicides into the region of the pustule—such as the tincture of iodine, phenol, and a solution of mercuric chloride. Excision, in addition to scar formation, has the additional disadvantage of laying open the blood and lymphatic channels so that symptoms of systematic infection may supervene and the operation by no means always terminates the local process.

The other methods are objectionable, because of the scar that is produced and because of the toxic symptoms which may follow them.

The use of anti-anthrax serum is recommended to displace these measures. The report of a case in which it was used is made by Joseph C. Regan<sup>7</sup> of Brooklyn. The patient was a man, 19 years old, who was admitted to the

(7) Jour. Amer. Med. Ass'n, June 14, 1919.

hospital with a diagnosis of anthrax. For the previous eight months the patient had been working in a factory in which hair brushes of various kinds were manufactured. His work had been mostly sweeping up the floor, handling hair, etc. On Friday, Dec. 27, 1918, he noticed a small red pimple on his cheek. It was not very painful and gave him no particular trouble. On the following day he began to feel more discomfort, his cheek began to swell considerably, and he could not lie on that side, owing to the pain in his neck. He visited a physician, who advised him to go to the hospital for treatment.

On admission to the hospital, smears and cultures were taken from the secretion of the vesicles and from the base of the pustule, by lifting up as far as possible the margin of the eschar. A blood culture was also taken. On the following day, December 31, smears and cultures contained anthrax bacilli. The treatment consisted of inserting a needle into the skin at the margin of the red areola and directing it fairly deeply into the subcutaneous tissues at the base of the pustule; it was then connected with a syringe and 12 c. c. of anti-anthrax serum were injected very slowly into these tissues in such a way as almost to circumscribe the pustule, the needle being of necessity inserted at three different points around the lesion. In addition, 30 c. c. of anti-anthrax serum were also injected intramuscularly into the buttocks. That night the temperature rose to 102° F. and the pulse to 110, evidently owing to the serum reaction.

The local injection of 10 c. c. of anti-anthrax serum and 30 c. c. intramuscularly was repeated. Three days later the patient had improved progressively. The cervical glands at the angle of the jaw had swollen to the size of small marbles and an injection of 10 c. c. of serum was made into the region of these enlarged glands. Cultures were again taken from the region.

January 4, four days after admission to the hospital, the patient's condition was very good. He was then up and around. He made a complete recovery.

The treatment used on this patient is recommended to replace the former methods as described above. Local measures must also be accompanied by suitable general treatment, however. Hence, serum should also be given

intramuscularly or intravenously in those instances in which it is given immediately around the region infected. Local treatment in order to effect a cure must anticipate the onset of anthrax septicemia.

**Fatal Case of Anthrax.** A fatal case of anthrax infection due probably to infection by a shaving brush, is reported by W. H. Norton and E. F. Kohman.<sup>8</sup> This was the third case of human anthrax at Camp Jackson, during a period of four months.

The patient in this instance was a private, 21 years old, who was admitted to the hospital complaining of slight headache, dizziness and backache. He was not acutely ill, having on the neck above the thyroid cartilage, an inconspicuous swelling without inflammatory areola, about 1 cm. in diameter, which he stated followed several days after the use of a new shaving brush. The leukocyte count after the second day's admission was 24,000. This increased to 31,000 on the following day. Three days after admission, the patient became nauseated and vomited a grumose material. The swelling of the neck had by this time assumed the appearance of a granuloma and the superficial chain of lymph glands along the anterior border of the right sternocleidomastoid muscle was enlarged. Around the granuloma was noted what was suggestive of a margin of dry vesicles. The center of the lesion showed beginning black necrotic change. There was no pain or tenderness about the lesion. The smear which was made from a freshly abraded surface showed organisms having the morphologic characteristics of the anthrax bacilli. The blood that exuded from the abraded surface turned black immediately. Anthrax bacilli were isolated and identified by an examination of material removed from the necrotic regions. Experimental animals died after injection of these bacilli and the organisms were recovered from these animals after death.

The patient died, and at autopsy the cause of death was found to be generalized infection with anthrax bacilli. The same organism was isolated from a shaving brush used by the patient at the time that he stated he injured himself.

(8) Jour. Amer. Med. Ass'n, April 19, 1919.



The following prominent points stand out from a study of this case:

An organism definitely shown to be the anthrax bacillus was found on a new shaving brush, the use of which was followed by a fatal infection. In all probability, this brush was the source of the infection. Attention is, however, called to the possibility of the shaving brush being infected by the granuloma on the patient's neck.

The clinical course of the disease was such that the diagnosis could not have been made without the laboratory examinations.

Intestinal carbuncles may be formed by a blood-stream infection as well as by the alimentary route. Of course, there is a possibility of the anthrax bacilli having gained entrance to the mouth at the time of shaving. However, the intestinal lesions were all, except one, covered by intact mucosa. Attention is called to the fact that these were all recent lesions in the intestine. It appears that there is a definite tendency for anthrax infections to localize in the intestine no matter whether the infection takes place by the blood stream, through the skin, or by the intestinal route.

## TETANUS

**Long Incubation Period in Tetanus.** The points of interest in this report are the long incubation period of a case of tetanus, severe reaction to serum treatment of the disease, with recovery from tetanus, and subsequent gangrene of the lungs, and death.

The patient was a man, 23 years old, a soldier, in the care of P. R. Cooper.<sup>9</sup> The patient was wounded by shrapnel on June 2, receiving numerous superficial wounds in the buttocks, right thigh and foot. His wounds healed after some slight complications, but four and a half months afterward he developed a choking attack, and while he was being examined by the doctor on this account, he sneezed, and it was the character of the sneeze which first aroused any suspicion as to the nature of the underlying disease at that time. It was as if the patient tried very hard to suppress the sneeze, but had

(9) Practitioner, March, 1919.

failed, and the effect of the sneeze was unduly long prolonged. There was spasm of the diaphragm, of all the respiratory muscles, and especially of the muscles of the neck and jaws. Sneezing was distinctly painful and he dreaded its occurrence.

On the following day, a diagnosis of tetanus was made, and the patient was given two doses of 30,000 and 10,000 units of antitoxin. When the second dose was administered the man suffered from severe anaphylactic shock. He recovered from the shock, and also from the tetanus, but was in a very greatly exhausted state after that. He then developed pneumonia, and finally gangrene of the lungs and died six weeks after the recovery from tetanus.

The striking features, as pointed out by Cooper, were: The long incubation period, assuming of course that the infection occurred at the time of the injury. Prior to the injection of antitoxin there had been only localized infection, although there was well-marked hypertonicity of the muscles of the trunk and lower extremities. The peculiar resistance and prolonged sneezing was very characteristic and has not, the author thinks, been referred to previously. Subnormal temperature, with profuse perspiration, was also notable. Collapse following a few hours after the intrathecal injection of serum was considered a true anaphylaxis, during which the patient almost died from respiratory and cardiac failure. The unfortunate development of a septic bronchopneumonia, which progressed to gangrene of the lungs, was presumably due to inspiration of septic material into the bronchi during the comatose stage, in which there was well-marked inspiratory dyspnea aided also, probably, by the lowered resistance to the anaphylactic shock.

**Fatal Tetanus After Injection of Gelatine.** This article is based upon the experience of F. Parkes Weber<sup>1</sup> with a patient who died of tetanus following a subcutaneous injection of gelatine, given as a hemostatic on account of grave intestinal hemorrhage in typhoid fever, in a man 25 years old, who was admitted to a hospital suffering with typhoid fever, and who on account

of severe intestinal hemorrhage was given a subcutaneous injection of coagulose and three hours later 2 pints of sterilized physiologic saline under the skin.

On the following morning for additional hemostatic effect, the patient was given 20 c.c. of gelatine under the skin, guaranteed to be sterilized for subcutaneous use. Two days later, 1½ pints of sterilized physiologic saline were again given subcutaneously. Five days after the gelatine was injected, the patient developed symptoms of tetanus and one day after these symptoms appeared he died, with a typical picture of tetanus infection.

At postmortem examination in addition to intestinal ulcers due to typhoid fever, there was a small abscess in the thigh at the site, apparently, of the gelatine injection and from this little abscess bacilli resembling those of tetanus were obtained.

Theoretically, it is possible that the patient with open intestinal ulcers might become infected with tetanus by way of these ulcers in the bowels. This, however, Weber considers extremely improbable in this or any other case. A sample of the gelatine used in this case was examined at the Lister Institute and was found to be contaminated with *Bacillus welchii* (*perfringens*) and the bacillus of tetanus morphologic type which gave a doubtful reaction in the presence of Type III tetanus agglutinating serum.

**Treatment of Tetanus.** Modern methods of treatment of tetanus are illustrated in the records of a single instance presented by M. S. Woolfe,<sup>2</sup> of the University of California Hospital.

He calls attention to the fact that there is still doubt in the minds of many as to the efficiency of antitetanus serum as a therapeutic measure.

Since the causative organism of the disease is anaërobic, it is probably most toxic when excluded from oxygen either by being in the deep tissues of the patient or in combination with anaërobic organisms, such as *B. subtilis* or *B. pyocyaneus*, which will exhaust any supply of oxygen present. *B. tetani* may be cultivated, however, in increasing supplies of oxygen until it finally

(2) Jour. Amer. Med. Ass'n, May 3, 1919.

loses its virulence. It may be locked up in a healed, and therefore sealed, wound for months and regain a practical toxicity during the advent of pyogenic organisms to a new wound, operative or otherwise, when tetanus symptoms disappeared months before; or, indeed, when no previous signs of tetanus had manifested themselves.

Reference is made to a case reported in the *British Medical Journal*, June 30, 1917, in which 200 days after injury, an operation was performed for bone grafting. Six days after this tetanus set in and three days later the patient was dead.

The patient whose record is presented here by Woolfe, was a boy 16 years old, who was accidentally shot with No. 12 gauge shotgun in the left thigh, at a distance of two or three feet. On the tenth day after the accident, he showed the first signs of tetanus; 25,000 units of antitetanus serum were given before he came under Woolfe's care, seventeen days after the injury, and seven days after tetanus symptoms were first noted. When first seen by Woolfe, the boy had marked trismus, retraction of the chest, gross Kernig signs, opisthotonos, board-like abdomen, generalized contracture of the body muscles, and a fine *risus sardonicus*, a late and serious sign of the disease.

Treatment was based on: first, the securing of rest, sleep and food; second, postponement of active interference with the wound until tetanus symptoms should disappear; and third, administration of antitetanus serum.

The patient was allowed to have any food he could handle and cared for, liquid or semisolids. Morphine sulphate, 0.01 gm. was given after meals, and every four hours for three doses. Chloral hydrate was prescribed the same day, 0.6 gm. every four hours, and at the end of the same day morphine sulphate, 0.008 gm. and chloral hydrate, 0.6 gm. became routine every four hours.

During the first fifteen hours of treatment, the patient had 19,500 units of tetanus antitoxin intravenously, and considerable nourishment. At times and simultaneously with the injection of serum he often obtained relief from chloroform inhalations; he was kept under chloroform as

long as an hour at one time. Night and day, every four hours, first 5,000 and later 10,000 units of antitoxin were administered almost entirely by the veins. In seven days the boy received 172,000 units intravenously. Improvement was noticed first on the ninth day. The temperature was normal on the tenth day. There were no symptoms on the twenty-fifth day, except local signs of a mildly suppurating wound which was, considerably later, curetted.

In commenting upon this condition, McConkey is quoted as saying that if one compares the mortality of all the cases treated with serum with that of the cases treated without, he must allow that the use of the serum brings little if any advantage, but if one compares the mortality of the cases treated with large amounts of serum, with the mortality of the cases treated with small amounts, then the beneficial results following such use of serum become manifest. This author is quoted as giving the figures of 51 and 70.2 per cent. as the recovery under treatment with small and large doses respectively.

In further comment upon this patient, Woolfe recalls that nearly all the antitoxin was given intravenously. He feels sure that if he had attempted to give a large dose of serum intraspinally six times a day, either he should have so stimulated the already critically sensitive reflexes to a point of the utmost danger, or should have had to endanger the patient's life with repeated administrations of chloroform or ether.

The patient reacted well to the antitoxin given intravenously. Woolfe considers that the intrathecal route is not the wisest in all cases; for rapidity of action, it is not so quick as the intravenous route. Intravenous anesthesia is no whit tardier than spinal anesthesia, and such anesthesia acts through the central nerve cells. The vascular system is more deliberate and more uniform in distribution than the casual administration of a fluid into the spinal theca. One intrathecal injection of antitoxin was used in this case, and subsequently the patient had more distress in the way of elevated temperature, more rapid respiration, and spasms than after any of the intravenous injections.



## RABIES

**Rabies and Its Treatment.** The nature of rabies and a description of antirabic treatment is presented by Sir David Semple,<sup>3</sup> of London.

In his introduction, the author describes an outbreak of rabies in England, and also discusses the terminology connected with the disease. Regarding the nature and localization of rabies virus, he says that all warm-blooded animals are susceptible to the disease. In ninety-nine cases out of 100 it means an infection of dogs, but there must also be considered cats, horses, cattle, foxes, deer, pigs and sheep, who may have rabies. In some parts of the Continent of Europe, wolves, jackals, monkeys and other wild animals also have rabies.

For practical purposes, attention is given to what happens when dogs are infected with rabies. This disease is a specific infectious one, the cause of which has not yet been discovered. In addition to being present in the saliva, which means that it is present in the salivary glands, infection is always present in the brain, medulla, spinal cord, cerebrospinal fluid, and the large nerves of man and animals suffering from rabies. It has been found in the pancreas and mammary glands and in some instances in the suprarenal capsules and the spleen, and there is some dispute as to whether it has been found in the blood stream. One author has claimed that placental transmission can occur.

The saliva of a dog may be infective for as long as five days, and in a few cases it has been found to be infective for six or seven days before any outward symptoms of rabies developed. These are points which should be taken into consideration in giving or refusing antirabies treatment to persons bit or licked on scratches or abrasions by dogs apparently healthy at the time, but which later have developed symptoms of rabies. Up to the present time all attempts to grow the virus that produces this disease on artificial media, or to stain and demonstrate it under the microscope, have not been accepted as successful.

Whether the bodies found in the medulla in cases of

---

(3) Brit. Med. Jour., Sept. 13-20, 1919.

rabies and generally known as Negri bodies are the cause of the disease, or only the result of cellular changes or alterations brought about by the rabies virus, has not yet been finally decided. The balance of opinion inclines to the view that they are cellular changes brought about by the rabies virus. Their presence in marked numbers in the brain of a dog or other animal suspected of rabies, is diagnostic of the disease.

In all animals susceptible to rabies, the disease manifests itself in one of two forms, namely, furious or delirious rabies, and "dumb" or paralytic rabies. The clinical picture presented by these two types is indicated by the name. In discussing the mode of infection, Semple says that the virus of rabies implanted in the wound by the bite of a rabid animal, or by the saliva coming in contact with wounds, scratches or abrasions, reaches the nerve centers, brain and spinal cord, by growing along the nerves from the seat of infection. On reaching the nerve centers, a period of fourteen days or thereabouts elapses before the first symptoms set in. The period taken by the virus in reaching the nerve centers is variable, depending on many factors, such as the individual's susceptibility, whether few or many or large nerves have been infected, and amount of virus implanted in the wound.

When the bites are on the face, hands or neck, the virus has only a short distance to go, along the nerves before reaching the brain. The object aimed at in anti-rabic treatment is to confer an active immunity against rabies before the virus of the animal which inflicted the bite reaches the nerve centers. When this has been accomplished the failures rarely exceed 0.5 to 0.8 per cent. and they may be even less than 0.5 per cent.

The first step in the treatment of bites by rabid animals is to cauterize the wound at the earliest possible moment. Undiluted phenol should be well swabbed into the wound and washed out with water immediately afterward. Crude phenol, undiluted izal, lysol or somewhat similar preparations, and iodine may be used in the absence of the first-named products. Caustic soda, caustic potash or silver nitrate are fairly good when well rubbed into the recesses of the wound, but they cause

considerable pain. Nitric acid and the red hot iron are barbarous methods and should never be used. Cauterization when thoroughly carried out within half an hour from the infliction of the bite will prevent hydrophobia in many instances, but not in all. When the tissues around the wound are incised there is always the danger of the virus in the original wound infecting the larger wounds made by the excision.

When a person is bitten by an apparently healthy dog in a rabies-infected area or country, certain precautions should always be exercised. In such a locality, bites of healthy dogs should receive the same local treatment as prescribed for the bites of rabid dogs. It is emphasized that the dog should not be destroyed but should be kept under control and close observation for ten days from the date of the bite, and in the event of any symptoms of ill health or departure from its normal habits, report should be made to the proper authorities.

If at the end of the ten-day observation period the dog is still healthy and free from any symptom of rabies, the person bitten has nothing to fear as regards infection. If the dog shows signs of rabies within ten days from the date of inflicting the bite, the person bitten should receive antirabies treatment as soon as possible after the condition of the dog has declared itself. A person severely bitten on the head, face, or neck, would not be justified in waiting ten days to know whether the animal was infective or not. The safest course to adopt in such cases is to commence antirabic treatment at once, and as soon as it becomes evident that the dog is not infective, leave it off.

In considering the incubation period of rabies it must be remembered that the variable factor here is the time taken by the virus in reaching the nerve centers by the nerve paths from the seat of infection. The earliest period at which a man or animal bitten by a rabid animal could show any symptom of hydrophobia or rabies would be fourteen days after being bitten. The disease manifests itself oftenest in the course of the second or third month after the infection, less frequently after the third month and rarely after the sixth month. The

nearer to the brain the wounds are situated, the shorter the incubation period.

The development of rabies in man is accompanied by certain symptoms which the author has never known to be absent, namely, an increase in temperature, a feeling of unrest, an appearance of excitement about the eyes and face and, most diagnostic of all, the inability to swallow fluid. At this stage patients may ask why they are unable to swallow, stating at the time that they are feeling quite well.

Pain in the region of the bite or in the limb in which it is situated, may or may not be present, but is probably more often present. The author has known it to be complained of in individuals severely bitten and who successfully underwent a course of antirabic treatment and remained well. It has not been established that recovery ever takes place in rabies of man or animal. Cases of alleged cure, or recovery in man are accounted for by a simulation of hydrophobia known as spurious hydrophobia, lyssaphobia, pseudo-hydrophobia, hysterical hydrophobia and, possibly, other names.

In most instances in hydrophobia toward the end of the disease, getting rid of the ropy saliva from the mouth and throat is a troublesome symptom, and attendants on patients should be warned about its infectivity. It gets on to the patient's hands, and when in a paroxysm he may scratch the attendants, or cough or expectorate on to their faces. These are possible methods of infections which would suggest themselves to any medical man attending the case.

Antirabic treatment is next taken up by Semple. He urges that persons bitten by rabid animals should appear for treatment as soon as possible, not a day, not even one hour should be unnecessarily wasted. Should the virus succeed in reaching the nerve center before immunity has been conferred, no treatment yet devised will save the patient.

The material used for antirabic treatment is prepared either from the spinal cords or from the brain, medulla and spinal cords of rabbits which have died from rabies after inoculation with "fixed" rabies virus.

The virus being of a fixed virulence may be termed a

vaccine when prepared for use, but the method of preparation differs in different Pasteur Institutes. Methods of preparation and administration are described in the article.

[As the treatment of rabies in America is carried out at institutes, or by physicians to whom the material and full instructions are supplied, it is not considered necessary at this place to go into detail concerning these points. The practitioner should promptly apply the needed early treatment in the attempt to destroy the virus in the wound and then send the patient to an institute for further treatment.—Ed.]



## DISEASES OF THE MEDIASTINUM

**Mediastinal Hodgkin's Granuloma.** The single instance of Hodgkin's granuloma, on which this article is based, is described by M. W. Lyon, jr.,<sup>1</sup> chiefly because of the mediastinal location, and the large size of the mass of new tissue and its pressure erosion through the anterior chest wall.

The condition produced as seen externally is shown in Plate II.

The patient was 20 years old. In April, 1917, he stumbled over a trunk and struck his chest on a cot; there resulted a swelling and soreness for several days, but no abrasion. One month later, there was a swelling at the site of the injury, or perhaps a little higher. This increased in size, enlargement was not painful. At this time he noticed shortness of breath on exertion and at drill. He entered the hospital Oct. 31, 1917. At this time a growth was found in the chest about 2½ inches above and to the inner side of the right nipple. A double plus Wassermann reaction was reported after an examination of his blood at the Army Medical School, and antisyphilitic treatment was instituted. This treatment produced no effect, however, and was soon abandoned. In April, 1918, the chest wall became perforated as shown in Plate II. Death from toxemic exhaustion occurred in August, 1918.

At autopsy, the mediastinum was found to be occupied by a large mass of new tissue, which extended into the right pleural cavity. This mass roughly measured 150 mm. in length by 75 mm. in width and thickness. It invaded and compressed the lung tissue on the right side, so that only about half the normal amount was present. What there was of the lung appeared necrotic and atelectatic. The large hard, yellowish gray mass extended firmly around the trachea and bronchi, as shown in Plate III, and invaded the neighboring lymph nodes which were enormously enlarged, firm and hard.

---

(1) Amer. Jour. Med. Sci., October, 1919.

On sectioning these enlarged nodes, they presented a light yellowish-gray color, and the larger ones were seen to have rather extensive soft necrotic centers. These nodes varied in size from about 5 mm. in the posterior mediastinum, to the very large mass of new tissue in the anterior part of the chest. Cervical and axillary lymph nodes were not enlarged. Many of the abdominal lymph nodes were enlarged and hard, resembling those of the thorax. Noteworthy among the glands so affected, were the superior gastric nodes, hepatic nodes and pancreaticosplenic nodes. The x-ray findings are shown in Plate IV.

From the posterior attachment of the diaphragm downward, the retroperitoneal nodes, including the iliac nodes, formed a more or less fused, solid irregular mass. The individual masses of new growth varied in size from 10 to 100 mm. in their greatest diameter. The inguinal nodes were also involved in this process, some of them having a diameter of 30 to 50 mm. Enlarged nodes could also be palpated along the inner aspect of the right thigh as far down as the knee.

The spleen, 120x70x45 mm., had the usual slaty purple color. Showing through the dark color of the organ could be seen, here and there, yellowish nodules. On section the bulk of the splenic pulp was found of an essentially normal dark reddish-brown color. In it were seen many yellowish nodules varying in diameter from 1 to 15 mm. There was no sharp line of demarcation between the splenic tissue and the tissue characteristic of Hodgkin's disease. The condition is shown in Plate V.

Nodules of the tumor tissue were found in the pancreas and the left kidney, the pericardium and myocardium, but none in the liver. Microscopic examination of the tissues removed at autopsy confirmed the diagnosis of Hodgkin's disease.

**Acute Leukemia and So-Called Mediastinal Leukosarcomatosis (Sternberg).** Among the various cases of leukemia there is a very characteristic though somewhat rare clinical and pathologic group, constituted by examples of so-called mediastinal leukosarcomatosis (Sternberg).

In this group there is a dense tumor-like mass in the

mediastinum, generally at the base of the heart, and apparently growing from the thymus gland, remnants of which may sometimes be found in the growth. The tumor-like growth tends to spread downward over the pericardial sac and to envelop it like a blanket.

The term "leukosarcoma" was introduced by C. Sternberg about 1905 for growths of this pathologic type, including chloroma and mediastinal leukosarcoma. They were or had been apparently regarded as a kind of sarcoma made of white lymphoid cells, which were constantly being thrown off in the blood stream, thus giving rise to a leukemic blood-picture in the circulating blood. These "lymphoid" cells were large non-granular uninuclear cells, more or less resembling large leukocytes, and though in some cases they might readily belong to the lymphocytic series of blood corpuscles and represent a "pre-lymphocyte" or lymphoblast stage, they might in other cases belong to the myeloid series and represent non-granular pre-myelocyte or so-called myeloblast stage, often giving a positive oxydase reaction.

Most cases of mediastinal leukosarcomatosis have not been recognized as such until the postmortem examination. F. Parkes Weber<sup>2</sup> in the present paper gives a summary of the findings in six patients who presented this condition. The first case was regarded merely as one of acute leukemia until the necropsy revealed the remarkable tumor-like mediastinal mass, including the remnant of the thymus gland, and enveloping a large portion of the pericardial sac. In a second case, the author was able with the help of Roentgen-ray examination and by microscopic blood pictures to make the diagnosis *intra vitam*.

The appearance of the tumor found in the mediastinum of these patients is indicated in the accompanying illustration (Plate VI).

The last patient referred to, one in whom a diagnosis was made during life, died, and the tumor in the mediastinum was typical of leukosarcomatosis, but an interesting condition was also presented by the kidneys. These were both enlarged and symmetrical in appearance. The medullary substance appeared at some parts

---

(2) Quart. Jour. Med., April, 1919.

imperfectly distinguished from the other pale cortical substance. Microscopic examination showed leukemic infiltration with cells of myeloblastic type, as in the liver. A most striking feature was that the hilus of each kidney, that is to say, the region outside the mucous membrane of the pelvis, which is normally filled up with connective tissue and hilus fat, was occupied by deep red spongy tissue; microscopic examination of this tissue showed it to consist chiefly of erythrocytes (hemorrhage) which evidently gave it its deep red color, and myeloid cells with large round or oval or grooved vesicular nucleus, and a moderate amount of clear cytoplasm free from neutrophile and eosinophile granules, apparently myeloblasts or "non-granular myelocytes," but some of these cells may have been lymphocytes. There were likewise a good many cells apparently myeloblasts which were undergoing mitosis, their nuclei staining more deeply and showing karyokinetic figures. Concerning the tissue found in the hilus of the kidneys, the author prefers the expression "myeloid substitution" or "myeloid replacement" to the term "myeloid transformation" or "myeloid metamorphosis," though the myeloid tissue may perhaps be regarded as bearing a relation to the fatty tissue normally present at the kidney hilus similar to that of the red myeloid tissue in the shaft of the long bones, in cases of red myeloid transformation of the yellow fatty bone marrow, to the yellow fatty bone marrow normally present (Plate VII).

In connection with this case Weber considers it clear that symmetrical leukemic hemorrhages occurred, and were associated with symmetrical growth of myeloid tissue at the hilus of each kidney. Until more is known of the true nature and causation of leukemia one can not definitely assert that the leukemic growths of myeloid tissue, whether in the bone marrow or in other extramedullary tissues and organs, can ever be regarded as having a conservative value, that is to say, as representing a vital reaction on the part of the affected organism, or a conservative supplementary nature.

In connection with the occurrence of symmetrical hemorrhages in myeloid leukemia, Weber refers to certain published reports of cases, in which patients in this

condition suddenly developed the symptoms of acute Ménière's disease. In one such case leukemic hemorrhage was found in both internal ears. The literature contains references to various similar cases and a few other cases of the same nature have been reported since 1905. The condition of the kidney removed in this case is shown in Plate 1 (Frontispiece).



## DISEASES OF THE BRONCHI AND UPPER AIR PASSAGES

**The Fate of Bacteria Introduced into the Upper Air Passages.** This investigation was carried out in the medical clinic of Johns Hopkins University Hospital by A. L. Bloomfield.<sup>3</sup>

By way of introduction he states that in considering the pathogenesis of infectious diseases in which the portal of entry is in the upper respiratory tract, three factors must be reckoned with. First, the means whereby the virus is conveyed to the individual; secondly, the fate of the organism from the time it reaches the mouth or nose until it is eliminated or until invasion takes place; and third, the actual invasion of the virus into the body.

Although many details of the mode of conveyance of bacteria from one host to another have been adequately determined, but little exact information is available about the localization, growth and disposal of such organisms, and the factors which determine a longer or shorter period of survival in the upper air passages before or after invasion has taken place. Studies of contact infection and of carrier incidence and persistence under various conditions afford indirect information, which is, however, inadequate to solve the detailed problems of particular infections. By actually introducing bacteria into the upper air passages in such a way that the dose, exact time and site of inoculation, and other conditions can be controlled, and by studying the fate of such organisms, it seems probable that knowledge of the details of the spread of bacteria, and of the development of the carrier state can be extended.

For the purpose of making this study an organism was sought which was not pathogenic, not normally present in the upper air passages of man, which could be readily grown on simple media, which could be easily

(3) Bull. Johns Hopkins Hosp., November, 1919.

recognized both in culture and in smear, and which would not be overgrown in culture by normal mouth flora. *Sarcina lutea* was selected as fulfilling these requirements.

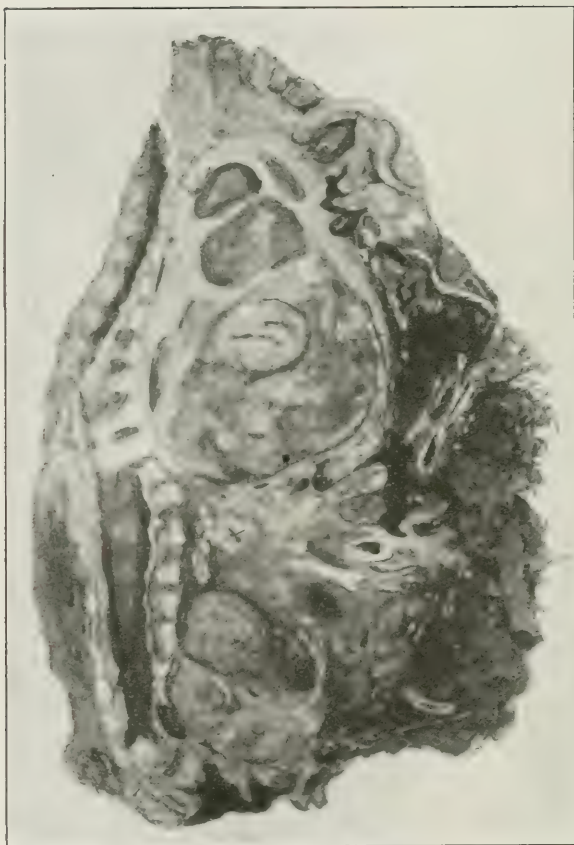
The method consisted in selecting individuals whose mouths and upper air passages presented no acute disease or abnormality other than those usually encountered and who would be regarded ordinarily as normal. The patient was kept under direct observation during the first hour of the experiment and for the most part took nothing by mouth during this time. Solid masses of a twenty-four hour growth of *Sarcina lutea* on plain agar were swabbed on the selected site, and cultures were taken at regular intervals thereafter. These intervals were 10 minutes, 1 hour, 24 hours and 48 hours after the inoculation. The cultures were made for the most part by scraping the mucous membrane with a heavy platinum loop, 0.5 cm. in diameter, and rubbing up the mucus obtained in this way in a loop of sterile salt solution. This was spread over several agar plates in varying dilutions. It was found that many more organisms were recovered by this method than by the usual swab technique. Detailed records of three experiments are presented.

In discussing the mechanism for disposal of bacteria in the upper air passages, it is stated that despite the frequent presence of pathogenic bacteria in the upper air passages, both in health and in disease, it is clear that a highly effective mechanism is present in these localities which, except under extraordinary conditions, protects against invasion by foreign organisms. A survey of the literature discloses studies on a number of factors which probably combine in making up the complex protective mechanism of the upper air passage. These factors may be classified as: (1) Mechanical, including the flushing action of secretions with the associated acts of swallowing and the ejection of nose and mouth secretions; (2) chemical, including the effects of the reaction of the mouth and nose secretions with other possible bacterial inhibitory factors; and (3) biologic, including such processes as phagocytosis and the effect of bacteria already present on the invader.



Perforation of chest wall by growth.—Lyon, page 258.

PLATE III.



New growth surrounding trachea and bronchus, invading and compressing lung.—Lyon, page 258.

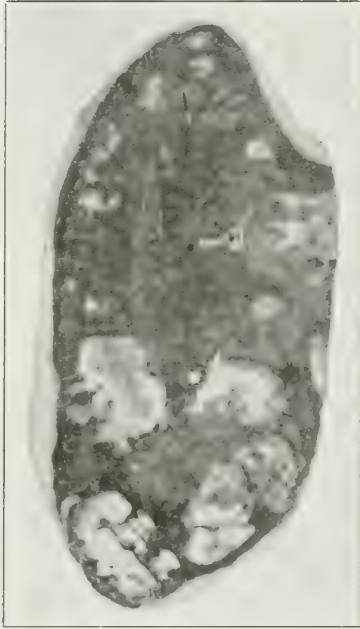
PLATE IV.



Roentgen-ray picture of growth in chest. Made by Major J. H. Selby,  
M. C., U. S. A.—Lyon, page 258.

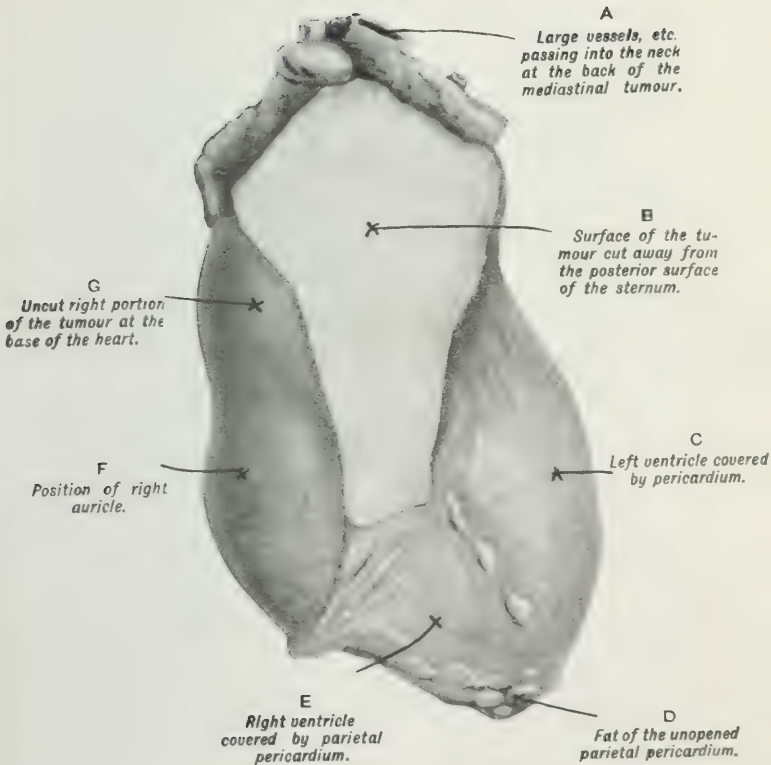


PLATE V.



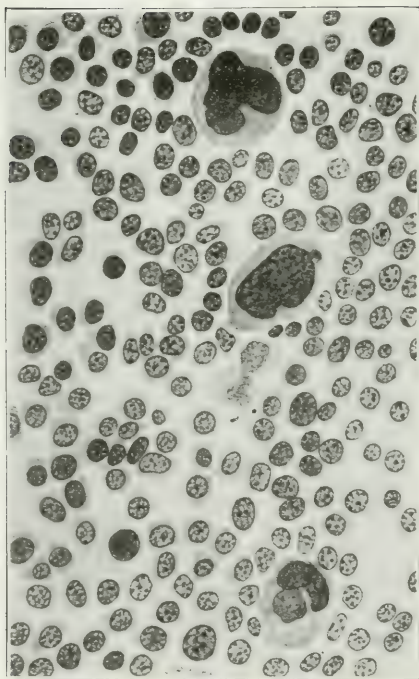
Section of spleen showing nodules of new tissues. — Lyon, page 258

PLATE VI.



Diagrammatic drawing (made directly after the necropsy) of the heart, covered by the unopened pericardium, with the tumor-like mass at its base. The anterior surface of the latter has been cut away from the posterior surface of the sternum. The drawing shows the relative positions of the heart and growth. Weber, page 259.

PLATE VII.



Microscopic drawing of part of the tissue (stained with hematoxylin and eosin) from the hilus of the kidney, showing myeloblasts and uninuclear and multinuclear bone marrow giant-cells (megakaryocytes). The erythrocytes were for some reason not stained, and are therefore not represented in the drawing. Magnification, 950.—Weber, page 259.

Results of the cultures made from the air passages of these patients are tabulated. The general result of the experiments indicates that even after a short period of time it is usually impossible to recover *Sarcina lutea* swabbed in large amounts on the tongue, nasal mucosa, or into the crypts of the tonsils. Disappearance from the nose was somewhat slower than from the other sites; in only one instance could any organisms be recovered after twenty-four hours, and in one case after two days. Cultures made in this way do not, of course, prove the complete absence of the organism in the mouth and nose, but the general trend of the quantitative relations indicates a rapid disappearance. The fact that the estimated dose of from 50 to 100 billion organisms was vastly greater than that in any natural infection indicates the remarkable efficiency of the mechanism present in the upper air passages for disposing of this organism. An analysis of the possible factors active in effecting this disposal indicated that reaction of mouth secretions, mechanical cleansing, and the mouth bacteria play little if any part, but that the saliva and mouth secretions exert a prompt and marked bactericidal effect. Similar methods are being used in studying the fate of other organisms introduced into the upper air passages.

**Horse Asthma Following Blood Transfusion.** A single instance of horse asthma following blood transfusion is reported by Maximilian A. Ramirez,<sup>4</sup> of New York.

The chief object of the report is to call attention to passive anaphylaxis in actual practice and suggest the necessity of including in the routine examination of a prospective donor for blood transfusion questions relative to various anaphylactic manifestations.

The patient considered here was a man 35 years old, a Greek, who underwent blood transfusion for primary anemia. He had never had asthma, hay fever, bronchitis, urticaria, angioneurotic edema, or any other conditions which might indicate a hypersensitiveness to some foreign protein. The family history was negative.

Two weeks after receiving 600 c.c. of blood, the patient went for a carriage ride, and immediately on enter-

(4) Jour. Amer. Ass'n, Sept. 27, 1919.

ing the open carriage, he experienced within five minutes a definite clear-cut attack of bronchial asthma. A physician was called and the attack was relieved by administration of epinephrine hypodermically.

When first seen by Ramirez, the man was tested against a large number of food and bacteria protein, pollens, etc., with negative result. Finally, however, a positive reaction to horse dandruff was obtained.

When the donor was questioned concerning his previous illnesses, he readily admitted being subject to a persistent and long-standing asthma and bronchitis. When he was tested, he was found to react to horse dandruff more acutely than did the recipient. This experience indicates that the transmission of anaphylactic or reaction bodies should be borne in mind in choosing a donor for blood transfusion.

The presence of these "anaphylactic bodies" in the donor's blood caused no untoward effect on the recipient during or immediately following the transfusion.

This phenomenon did not occur in another patient to whom this donor had previously given blood, although a larger quantity of blood was injected, 800 c. c.

**Treatment of Bronchial Asthma with Vaccines.** This discussion of the treatment of bronchial asthma with vaccines by I. Chandler Walker,<sup>5</sup> of Boston, is a continuation of the work that has been abstracted previously in the Practical Medical Series.<sup>6</sup> The present paper concerns those patients who were treated with vaccines and represents a total of 178 individuals, twenty-eight of whom were sensitive to bacterial proteins, and therefore were treated with vaccines of the organisms to which they were sensitive. The remaining 150 patients included in the paper were not sensitive to any proteins with which they were tested. Cases in which the patients were not sensitive to proteins were thought to be of an infectious type and the infection was considered to be in the respiratory tract. Therefore, vaccines were made from the organisms found in patients' sputum or nasal secretions. Since these sources produced such a wide range of bacteria it was thought best and simplest to find

(5) *Archiv. Int. Med.*, February, 1919.

(6) *Practical Medicine Series*, 1919, Vol. I. p. 199.



out first what part those organisms which only grow in plain agar might play in the cause of bronchial asthma; second, what part of those organisms which grow only in dextrose bouillon and not in plain agar might play.

It was learned that some patients were relieved of asthma by plain agar vaccine, and others were relieved by bouillon vaccine; but still there were many in each group who were not relieved. Therefore, a series of patients were treated in both ways. The patients who were sensitive to bacterial proteins and treated with vaccines are considered first. The treatment was given with whole killed bacteria in the form of a vaccine because by so doing the patient would be apt both to acquire an immunity to the bacteria and to become desensitized to the protein of the bacteria, whereas treatment with the protein of the bacteria alone would only desensitize and not immunize.

Cultures made of sputum and secretions from these twenty-eight patients yielded *Staphylococcus pyogenes aureus*, *Streptococcus hemolysans* and *Streptococcus viridans*, for the most part. Diphtheroid bacilli were found in some instances and were found to be valuable as a part of vaccine used in the treatment of the patients from whom they were derived.

The next division of the work has to do with seventy-five patients who were treated with vaccines made with the bacteria which were recovered from the patient's thick sputum when the sputum was streaked on large surfaces of plain agar. The types of organisms recovered from the sputum and incorporated into vaccines in these seventy-five patients were chiefly *Staphylococcus pyogenes aureus* and *S. albus*, a diphtheroid organism and, in a few instances, Friedlander's bacillus.

Still another group includes all those patients whose sputum when inoculated into dextrose bouillon grew types of organisms which resembled a streptococcus morphologically, and which in addition were Gram-positive staining and bile-soluble. Therefore, in these patients the predominating organism when the sputum was grown in dextrose bouillon was probably a streptococcus, although no attempt was made in these instances to identify the particular type of streptococcus and vaccines

were made directly from the dextrose bouillon cultures after from twenty to twenty-four grows by centrifugalizing out the bacteria, washing in normal saline, and then suspending the washed bacteria in normal saline.

There remains still a group of non-sensitive patients treated with several different vaccines. The patients in this group were not only treated with the predominating organisms in the sputum when it was grown on plain agar and in dextrose bouillon, but also, if the patient was not relieved by such vaccines, other types of organisms were employed. In other words, vaccines of different types were tried, one for a period of several weeks until the proper one was found, and relief, or marked improvement resulted.

In considering the group of summer asthmatics, Walker says that it is generally believed that the type of asthma which is limited to the summer months is caused by pollens. There should be some discussion of the sixteen patients who were not sensitive to pollens although their attacks of asthma closely paralleled the pollination of plants. These patients were given vaccines made from the organisms used on patients of the previous groups. Of the sixteen patients in this group of non-sensitive summer asthmatics who were given vaccines, five were relieved of asthma, four were markedly improved, four were not benefitted, and three were not treated.

The results of this work are recorded as follows:

Twenty-eight patients with bronchial asthma were treated with vaccines of the bacteria to which they were sensitive; 75 per cent. were relieved of asthma and 21 per cent. were improved.

Seventy-five non-sensitive patients were treated with vaccines made from culturing the sputum on plain agar; the predominating organism was usually the one selected for treatment: 46.6 per cent. were relieved of asthma and 15 per cent. were improved.

Twenty-four non-sensitive patients were treated with vaccines made from culturing the sputum in dextrose bouillon and using only the streptococci; 37.5 per cent. were relieved of asthma and 25 per cent. were improved.

Thirty-five non-sensitive patients were treated with vaccines made from culturing the sputum both ways; in

other words, vaccines of many types were used; 31.4 per cent. were relieved and 23 per cent. were improved.

Sixteen non-sensitive summer asthmatics were treated with vaccines; 31.2 per cent. were relieved and 25 per cent. were improved.

Therefore, of 150 non-sensitive asthmatics who were treated with vaccines, 40 per cent. were relieved and 20 per cent. were improved. These results should be compared with the treatment of sensitive patients as reported in the previous article, 75 per cent. of whom were relieved.

With the sensitive cases, the age of onset of asthma, the duration of asthma and the age of the patient when treated had little to do with the prognosis; however, with the non-sensitive cases these facts had much bearing on the prognosis; the older the patient is when asthma begins and the older he is when treatment is begun the more unfavorable the prognosis from vaccines in non-sensitive cases.

The permanency of relief from vaccines in the non-sensitive cases depends on the individual's resistance to the bacteria in question; therefore, the duration of relief from asthma varies. Some patients continue free from asthma after vaccines are discontinued for many months, others for only a month or two, and some patients require the constant use of vaccines to be free from asthma. Succeeding courses of vaccine treatment, provided that there has been no change in the bacteria which are causing the relapse, seem to relieve more promptly than the first course of vaccine treatment. When a relapse is not relieved by a second course of vaccines which previously did relieve, other bacteria should be suspected as the cause of asthma and new vaccines should be made.

**Treatment of Bronchial Asthma with Pollens.** This paper by I. C. Walker<sup>7</sup> deals with the treatment with pollens, preceding the pollen season, and during the pollen season, pollens as the possible cause of continuous asthma, the specificity of proteins in the treatment of bronchial asthma in conjunction with multiple sensitization, the association of hay fever with bronchial asthma,

(7) Amer. Jour. Med. Sci., March, 1919.

and the kind of pollens with their respective seasons that are the cause of bronchial asthma.

Before a patient can be treated with the pollens, it is necessary to know how sensitive that patient is to the pollens, therefore different strengths of the solutions of the pollen protein are used.

These solutions are made as follows: To 0.5 gram. of the dry pollen are added 44 c.c. of sterile normal saline and the mixture is shaken thoroughly at frequent intervals for twenty-four hours, after which enough absolute alcohol (6 c.c.) is added to the mixture to make the alcohol content 12 per cent. Again, the mixture is thoroughly shaken at frequent intervals for twenty-four hours, after which it is centrifugalized at high speed and the supernatant fluid is pipetted off and saved. This supernatant fluid therefore consists of the pollen protein dissolved in a 12 per cent. alcoholic-normal saline solution, and it represents, by weight, 1 part pollen to 100 parts solvent. This 1 to 100 solution is used as stock and from it other dilutions, 1 to 500, 1 to 1000, 1 to 5000 and 1 to 10,000 are made. These solutions are used for the skin tests and for treatment, and with the addition of a small crystal of thymol they keep for many months in a cool place.

The method of treating with the pollen extracts follows: The first treatment consists of 0.1 to 0.2 c.c. of that dilution next higher than the one which gave a positive skin test; or, in other words, the first dose is 0.1 c.c. or 0.2 c.c. of the strongest dilution which failed to give any skin reaction whatever, no matter how slight.

With the pollen extract used by Walker, the majority of patients treated gave a more or less positive reaction with the 1 to 5000 dilution, therefore the first treatment consisted of 0.1 c. c. or 0.2 c. c. of the 1 to 10000 dilution. Treatment was given subcutaneously once a week.

Walker has found by experimentation that the following is the best outline of treatment for a patient who gives a more or less positive skin test, with a 1 to 5000 dilution of pollen extract: 1 to 10000 give 0.2 c.c., 1 to 5000 give 0.2 c.c., 0.3 c.c., 0.3 c.c., 1 to 1000 give 0.2 c.c., 0.3 c.c., 1 to 500 give 0.2 c.c., 0.3 c.c., 0.4 c.c., 1 to

100 give 0.1 c.c., 0.2 c.c., 0.3 c.c., each dose to be given preferably at weekly intervals.

The subject of pollen treatment preceding the season follows. By this is meant treatment that is completed before the season of pollination of the particular plant begins, for instance immunization against timothy and redtop; should be attempted in treatment that should stop about the end of May. Treatment directed at immunizing a patient against summer asthma would be completed by the middle of August, because this type of the disease comes on about the middle of August, and continues until the first frost, usually early in October. This season represents the pollination of the ragweed, which is the cause of practically all the pollen asthma of this season.

The results of treatment of thirty-one patients according to the above plan are presented and are encouraging.

From these cases it is also shown that in order to prevent asthma caused by pollens, by treatment preceding the season, two or three treatments with the 1 to 100 dilution should be given. According to the plan for dosage described above, one must allow for at least twelve weeks during which one treatment a week is given, and which will be finished before the pollen season of the offending plant opens.

After a completion of a series of treatments as outlined above, the cutaneous tests with the pollens with which treatment has been given is greatly reduced in positiveness. A year later, however, these same patients give practically the same degree of positiveness with the skin test as they did previous to treatment the preceding year. Much more treatment would be necessary absolutely to desensitize, consequently the patients prefer to repeat the shorter series of treatments each year.

Treatment with pollens during the season of pollination must be carried out with the greatest care, since during such treatment the patient is not only being injected with the pollen, but is at the same time also being exposed to the pollen in Nature.

During the pollen season, treatment must be begun with such an amount that fails to give any reaction what-



soever to the skin, and yet if too small an amount is given there will be no benefit.

Tabulated results are presented that show that much greater success is obtained by treatment preceding the season than by treatment during the season. Nevertheless, if the former cannot be done, the latter is worth trying. Both methods of treatment should be employed in the same patient provided the treatment preceding the season fails.

Walker concludes that in the treatment of pollen asthma there are only two methods available. The best method is to give sufficient treatment preceding the season of pollination and then stop, and by sufficient treatment is meant to begin treatment three months ahead of the season, so that the few final treatments will be with the strongest dilution of the pollen protein (that is, the 1 to 100 dilution). If this method happens to fail, treatment may be continued through the season, but the dosage must not continue on the increase from the amount last given; the dosage must be dropped back to the original first dose and very cautiously increased. The only other method worth doing is not to give any treatment preceding the season but wait until the patient begins to have asthma, then treat cautiously; first give one or more doses of the highest dilution which fails to give any reaction whatsoever on the skin and very slowly increase the succeeding doses. It is far better to give two doses that are so small that no improvement results before a beneficial amount is given than to run the risk of giving too large an initial dose, which may upset the patient and thus discourage the physician.

The next subject considered is pollens as a possible cause of continuous asthma. Frequently patients who have asthma more or less continuously throughout the year give a history of the onset of asthma or of the first attack during some summer months when some flowers are pollinating and they also give a positive cutaneous test with the pollens of that particular season. Frequently asthma does not stop when the season of pollination is over, but persists for several months. Other patients in whom the pollens are less suspiciously the cause of continuous asthma state that the asthma

although continuous throughout the year is much worse during certain months, and they give positive skin tests with the pollens which are prevalent at the particular time. The question as to what prolongs the asthma after the primary cause ceases to exist naturally arises. The answer is that various other causes prolong the asthma, and one of these is bacteria as a secondary invader. Other causes which may prolong a pollen asthma are specificity of proteins and multiple sensitization and various causes for the prolongation of pollen asthma.

The association of hay fever with bronchial asthma is a common occurrence. Frequently hay-fever patients have a very slight attack of asthma at some time during the hay fever, often the hay-fever symptoms end with a day or two of asthma, and still other patients are more or less choked up at times during their hay fever. None of the latter cases is included in this paper, because the amount of asthma was too slight, and the attack too unreliable to claim benefit or relief from treatment. These cases do, however, show the frequent association of hay fever and asthma when caused by pollens. Wæ'ler points out that there are three definite pollen seasons. The first occurs in April and May, when the various trees pollinate: among the first to pollinate during this season are the willow, birch and maple, and the last one to pollinate is the pine, which occurs the last day or two in May. Although the pollen of any of these trees may cause asthma, the author has had only one case caused by willow, one by birch and one by pine pollens. The second pollen season, and a more important one, occurs during June and July. The principal plants which pollinate at this time are the rose, June grass, orchard grass, redtop and timothy. The rose and orchard grass are not frequently the cause of asthma. June grass is so similar, botanically, to redtop that it is not used in the author's tests. Practically every patient who is sensitive to timothy is also somewhat sensitive to redtop, usually less so.

The third pollen season, and by far the most important, occurs during August and September, and the important pollens at this time are those of ragweed, goldenrod and daisy. Ragweed is practically always

the cause of pollen asthma at this season. It is emphasized by Walker that some patients have so-called asthma during June and July, others during August and September, and still others have so-called asthma throughout the summer, but they are not sensitive to pollens, and the asthma in these cases is caused by bacteria. Therefore, it is essential to do the skin or cutaneous test in all cases of summer asthma, and it is, he says, ridiculous to treat all summer asthmatics with pollens. Furthermore, it is unnecessary and possibly harmful to treat pollen asthmatics with an extract composed of many pollens, such as in the past has been put on the market by commercial firms when the patient actually requires only one or possibly two varieties of pollen. Attention is called also to the fact that occasionally the pollen seasons vary in time depending on weather conditions.

In conclusion the author states that readers of this paper should bear in mind that he collected his own pollens and made his own preparations by the method outlined above and that his results depend upon this fact. The results will naturally be specifically true only when these methods are followed and with those who purchase individual pollen preparation which are comparable with those prepared in this work.

**Review of Bronchial Asthma.** A considerable portion of this article by W. C. Thro,<sup>8</sup> of the Department of Clinical Pathology at Cornell Medical College, is taken up with a brief review of the literature on the subject.

In his own practice, Thro has tested thirty patients with bacterial protein and found very few positive reactions, and these were not marked. On the other hand, he points out that Walker considers the cutaneous tests to have been proved of value in determining a bacterial cause in some patients.

In those who are non-sensitive to the abrasion method it is possible that the intradermal test would demonstrate bacteria as the causative factors in some asthmatics. Thro advises, however, that in testing patients to get an idea of their sensitiveness to proteins, practitioners should use the skin abrasion method, the intradermal test being too sensitive. In using the skin

---

(8) New York Med. Jour., March 22, 1919.

abrasion method, thoroughly clean the flexor surface of the forearm with 55 per cent. alcohol, and with a small pipette or a platinum loop place a drop of decinormal sodium hydrate near the antecubital space, and below to one side place another drop. With a von Pirquet borer or a Hagedorn needle the skin is abraded through the first drop and this is used as a control. The skin should not be made to bleed. To the second drop there is added with a small platinum spatula a small amount of the dried protein to be used and the skin is abraded here also.

The patient should be questioned as to sensitiveness to substances and thus the test may be expedited. A very positive reaction appears within a few minutes and consists of a wheal at least 1 cm. across, with a sharply demarcated, raised and jagged border, and this wheal may be surrounded with an area of erythema. In some cases, the reaction may be positive, although there is only an excessive erythema. But, of course, it must be much larger than the control. When good strong reactions are obtained, they are truly remarkable and convincing. The author has tested thirty-four patients with bronchial asthma, or with chronic bronchitis, and three with hay fever. He used thirty-two proteid substances and two pollens—ragweed and timothy. Of the thirty-two proteid substances, four were bacterial made by himself. They were made from *Streptococcus viridans*, *Streptococcus hemolysans*, *Staphylococcus aureus* and a chromogenic Gram-negative coccus isolated from the sputum of an asthmatic patient. The bacterial proteids were made from microörganisms grown on agar, from which they were removed, washed with saline twice and then washed with alcohol containing phenol twice, and finally washed with ether and then allowed to dry.

Of the thirty-four patients, three reacted to the chromogenic Gram-negative coccus, one reacted very slightly to *Streptococcus hemolysans* and one reacted very slightly to *Streptococcus viridans*. Two gave a marked reaction with dog's hair; one gave a slight reaction with cat's hair; one gave a very slight reaction with horse dandruff; and none reacted to egg yolk. Thirteen patients were tested with egg whites, of these

one gave a very marked reaction; ten were tested with cow's milk, and one gave a marked reaction. A few asthmatics were tested with the common cereals, and one patient reacted strongly to these. One was found to give a strong reaction to fruit protein, a substance isolated from banana. One moderate reaction was obtained by using protein isolated from lobster.

In discussing the therapy of asthma, Thro says that patients sensitive to protein of horse dander, dog's hair, cat's hair and pollen, are relieved by a process of desensitization. It is unfortunate that the effects are transitory, especially with hay fever, and that consequently every year the patient has to go through a series of prophylactic inoculation before the appearance of the causative pollen. With patients sensitive to food proteins, it seems that the only course is abstinence from the food which causes the disagreeable reactions.

As to vaccine therapy, it seems to be the consensus of opinion of several investigators that some of the patients are relieved by injections of vaccines.

**Anaphylactic Death in Asthma.** A record of anaphylactic death in an asthmatic patient is published by T. H. Boughton.<sup>9</sup>

He states that in the literature there are reports of nine cases of bronchial asthma with postmortem records. In none of these cases is the exciting cause of the asthmatic attacks mentioned. It is impossible to show any direct relationship between these cases and anaphylaxis.

The case reported by Boughton occurred in a man, 29 years old, who for ten or twelve years before his death had been subject to attacks of bronchial asthma when in proximity to horses.

He was well informed on the subject and was anxious to have a desensitizing dose of horse serum, although he was familiar with the danger. He was taken to a hospital and one minim of horse serum was administered intravenously. Within two minutes a typical attack of asthma supervened. He was given 10 minims of epinephrine (adrenalin) intravenously, with definite relief for about 10 minutes. In all, 50 minims of epinephrine were given in five doses intravenously. Each gave re-

(9) Jour. Amer. Med. Ass'n, Dec. 27, 1919.



lief for several minutes, but eventually the patient died 45 minutes after the injection of serum. Postmortem was performed within an hour and a half after death.

The essential findings at autopsy are brought out in the author's comments. Special interest lies in this case, he says, because of the relation to the recently popularized desensitization method of treating those patients who have asthma (and of certain other clinical conditions) and who show sensitization to specific protein. Undoubtedly this patient should have been treated with high dilutions of serum as advocated by Walker instead of the undiluted serum.

Further interest also lies in the small quantity of serum used which produced death. Of the other recorded cases, probably the Langerhans case (in which 1.2 c.c. of serum were used) involved the smallest amount of serum.

A third point emphasized is the striking similarity in appearance of the organs in this case to those of experimental anaphylaxis in animals. The enormous distension of the lungs, the intense passive hyperemia of the abdominal organs, and the occasional subserous hemorrhages are highly characteristic of experimental anaphylaxis.

Furthermore, this is the only case of death from acute anaphylaxis uncomplicated with morbid conditions that the author has been able to find in which microscopic studies were made. Koch reported necropsy findings in a case of anaphylaxis in a child with scarlet fever and suppurative tonsilitis, but the microscopic findings are all referable to the infection present.

In the present case, a condition is presented in which repeated anaphylactic shocks have been experienced, and thus an opportunity is afforded to study the accumulative effect of this intoxication. Undoubtedly, the repeated asthmatic attacks to which this patient was subject, did not mean so severe an intoxication as is usually experienced by laboratory animals in experimental work. Yet, it is interesting to note that the edema, degeneration and necrosis of the epithelial cells of the liver and kidneys and the thickening of the arterial walls in the spleen, liver, lung and heart correspond closely to the

changes that have been described in experimental chronic anaphylaxis.

Boughton points out also that it has been well known for a number of years that one must exercise extreme care in giving curative serums to asthmatics. No satisfactory method of desensitization has yet been discovered to make safe the administration of serum to asthmatics with acute infections, such as diphtheria, in which time is such an essential factor in treatment. Besredka's method of "*dosès subintrantes*" has not justified the claims originally advanced for it, and Weil has pointed out grave objections to its use as a routine procedure. At best, the methods of desensitization are uncertain. In experimental work, animals sensitized with a small dose of serum can be desensitized with a small dose. Animals sensitized with a large amount of serum require a relatively large amount to effect desensitization—an amount, indeed, that would be fatal to an animal sensitized with a small dose. Since we can not know whether man should be desensitized by a large or a small dose, this method is unsatisfactory for practical use. The giving of a series of doses of gradually increasing size may, in some cases, produce desensitization, but in others it will bring on a fatal attack of anaphylaxis instead. Of course, the intravenous method of administration in these cases is more dangerous than the subcutaneous; and yet in only a small number of cases is the danger great.

## BRONCHIECTASIS

**Differentiation of Bronchiectasis from Pulmonary Tuberculosis.** The multifarious lung lesions produced by the tubercle bacilli, and the extreme variation in the clinical course of a given group of cases have influenced physicians to attribute signs in the lungs deviating from the normal, to phthisis pulmonalis, the common disease, when in reality, such signs, when carefully analyzed, after the history of the case is accurately ascertained, are found to be due to pathologic changes, non-tuberculous in character.

In view of the growing tendency to isolate the "ad-

vanced consumptive," such patients have frequently been banished to hospitals for the tuberculous before the nature of the disease in the lungs had been definitely determined.

To avoid such occurrences, various chronic lung affections simulating pulmonary tuberculosis must be carefully studied. Chronic non-tuberculous lung infection, involving the lower lobe or the upper lobe of each lung, such as syphilis of the lung, or chronic bronchitis and heart conditions may give rise to signs and symptoms that resemble tuberculous infection closely. Yet, surprisingly little has been said of bronchiectasis in making a study of those diseases which are confused with tuberculosis.

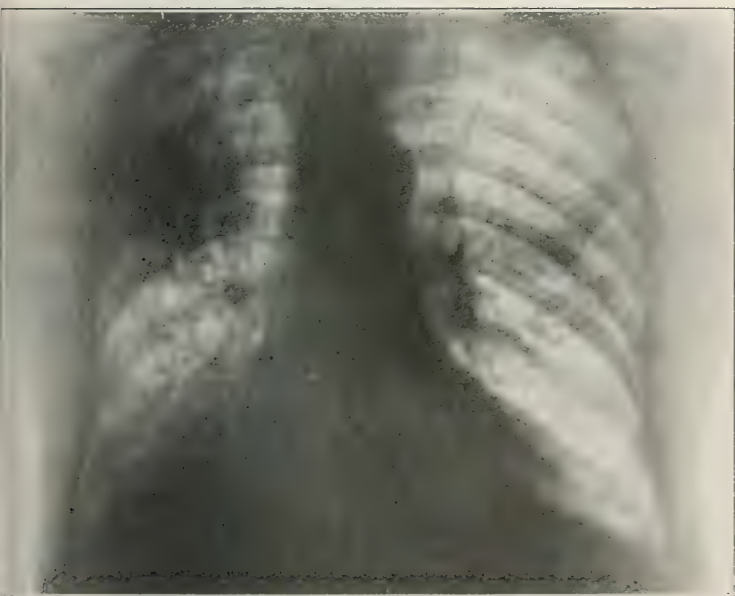
It is this subject of differentiation between bronchiectasis and pulmonary tuberculosis that is considered by B. Stivelman,<sup>1</sup> who points out that bronchiectasis will rarely, if ever, be confused with acute progressive types, but that it will be confused with tuberculosis characterized by mild constitutional symptoms, little or no wasting, and with physical signs suggestive of marked fibrosis. The patients with bronchiectasis, the study of whose cases was made the basis of this article, were treated at the Montefiore Home Country Sanitarium, Bedford Hills, New York. They constitute only a few of those patients sent to this institution as advanced consumptives. The author considers that among the more difficult to diagnose are those cases in which there is an elevation of temperature in the afternoon hours. It must be remembered, however, that afternoon rise of temperature is not uncommon in the older bronchiectatics. In arriving at a diagnosis in these patients, the history of the disease is of great importance. It will most usually disclose absence of early constitutional symptoms of toxemia, and fair health in spite of the distressing cough and profuse expectoration. The physical examination will reveal an unilateral lesion most frequently involving one of the lower lobes. Repeated examination of the sputum will not show the presence of tubercle bacilli. Stivelman presents, as an example, the record of a patient with late bronchiectasis, with mild

(1) Amer. Jour. Med. Sci., October, 1919.

constitutional symptoms due to retention of secretion with autopsy findings. This patient was a woman, 66 years old, who had had measles and cholera in infancy, pneumonia at six years of age and again three years before her admission to this institution. She had had frequent attacks of grippe since her last illness. She had not been well since an attack of pneumonia three years previous to her admission. Expectoration at first had been scanty, then became profuse, and pain was soon complained of in the lower part of the right chest posteriorly. Because of the history of pneumonia immediately preceding the present complaint, and the absence of fever in the early stage of the disease, comparatively slow pulse, the profuse and periodically fetid expectoration, fair nutrition, with a history of cough of three years duration, the negative findings in the profuse expectoration and the absolute unilateral involvement, more marked at the lower lobe, the diagnosis of bronchiectasis was made and the patient was transferred to a non-tuberculous ward of the hospital. There she grew progressively weaker, and began to show signs of right heart insufficiency and died eight months after admission. At autopsy the diagnosis was confirmed. The condition of the lung is shown in Plates VIII and IX.

Bronchiectasis complicated with pleural effusion is next discussed. This condition is one of the most frequent complications of pulmonary tuberculosis. In doubtful apical lesions, the occurrence of an effusion frequently clinches the diagnosis of tuberculosis, whether or not tubercle bacilli are found in fluid aspirated either microscopically or by animal inoculations. But an effusion superimposed on a pulmonary lesion of the lower lobe is not necessarily tuberculous. In bronchiectasis the abundant fetid sputum is free from tubercle bacilli. Furthermore, it is exceedingly rare to find a unilateral far-advanced tuberculous lesion while bronchiectasis is most frequently unilateral and almost always involves the lower lobe. Pulmonary osteo-arthritis is most marked in bronchiectasis, and the general health of these patients suffers but little in spite of the distressing cough and profuse expectoration of many years duration. Hemoptysis at times leads to further con-

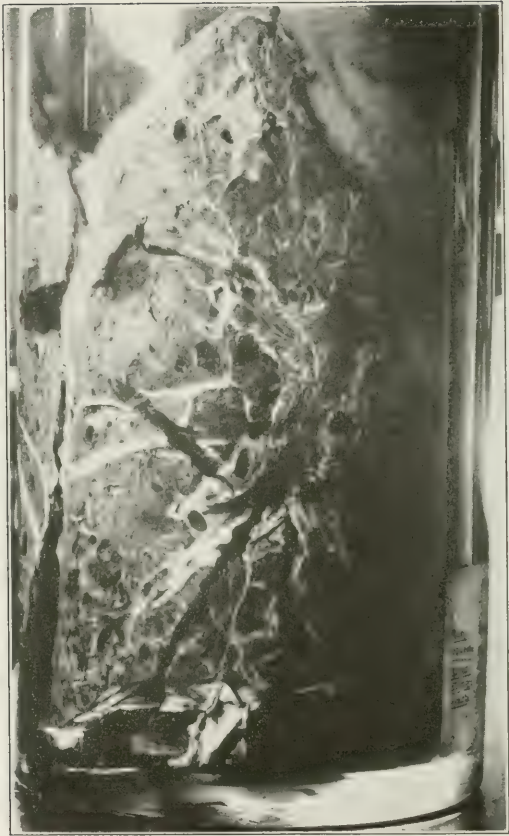
PLATE VIII.



Left lung: Marked hilus changes; otherwise negative. Right lung: Diffuse infiltration throughout the lung most marked at the middle lobe with evidence of a great many dilated bronchi. Heart moderately enlarged and slightly pulled to right. Arch of aorta moderately dilated. Evidence of pleuropericardial adhesions.—Stivelman, page 278.



PLATE IX.



Note the various sized cavities throughout the lung. One large cavity communicates with a bronchus (split open) at the middle lobe. —Stivelman, page 278.

fusion in differentiating bronchiectasis from tuberculosis. Hemoptysis is at times the first and only symptoms of phthisis. It must be remembered, however, that fatal cases of hemoptysis of non-tuberculous origin are seen fairly often; it occurs almost as frequently in bronchiectasis as in pulmonary tuberculosis. The concomitant marked pulmonary osteo-arthritis, the lack of constitutional symptoms in the early period of the disease, the negative findings in the sputum, the exclusive unilateral and lower lobe involvement, clear apices on Roentgen-ray examinations, the comfortable and active mode of life in spite of the long duration of the disease, will point toward bronchiectasis as producing the existing conditions.

In discussing the location of bronchiectasis, the author points out that the upper lobe is involved but rarely, and a differential diagnosis from phthisis pulmonalis requires careful study and a long period of observation. Signs of excavation elicited over an upper lobe are almost invariably due to pulmonary tuberculosis. Pulmonary abscess is encountered, but it is very rare, indeed, and can be diagnosticated with little difficulty.

## BRONCHIAL SPIROCHETOSIS

**Bronchial Spirochetosis (Castellani).** This study, by N. Farah,<sup>2</sup> is based on a series of ten cases, though many more patients were treated. The causal organism, *Spirochaeta bronchialis*, was discovered in Ceylon, in 1905, by Castellani. Since then it has been found in various places both in the tropics and in temperate zones, and Farah believes that it is very common and world-wide in its distribution (Fig. 6).

In each sample of sputum, search was made for the spirochete, the tubercle bacillus, eggs of *Distoma westermani*, and moulds. Out of twenty-eight suspects there was bloody expectoration at some time in twenty-four. In the twenty-eight cases, the spirochete was found in ten (in seven with blood-tinged sputum); the tubercle bacillus in fourteen; Pfeiffer's bacillus in two; and *Monilia pinoyi* in two.

(2) Presse méd., Dec. 17, 1919.

The *Spirochaeta bronchialis* stains readily with basic aniline dyes, coloring easily by Ziehl's method, carbolfuchsin violet and crystal violet. It is Gram-negative. In each preparation the parasite was found in considerable numbers, in fact swarming. Most were seen in Case 10, in which there was no hemoptysis; here the entire field was completely covered.

From a morphologic point of view, the organisms found exhibited spirals varying in length, shape and number. The length ranged from 2 to 35 *microns*, usually from 5 to 15. The shape varied from thick to very thin, the ends were swollen or tapering. The thick organisms are less numerous.

Cytologic examination of the sputum showed nothing very characteristic; and except four slight cases of eosinophilia, the blood was negative, as were also the Wassermanns and urinalyses.

As regards age, the ten patients varied from 20 to 45 years. Only two cases were acute, in the others there was chronic cough. The general condition was unchanged. Appetite was good. In practically all the cases, acute or chronic, there was frequently a sensation of intrathoracic oppression.

Cough began either in an acute manner, or insidiously and varied in gravity. As a rule it was more marked on waking, in the evening and at night than in the daytime. In one patient, cough lessened in winter, and reappeared in spring; another had but slight cough, though a constant hawking was necessary to clear the throat; in a third, hemoptysis was the initial symptom.

The expectoration varied greatly as to quantity and characteristics—in one scanty, in another moderate or profuse, viscid or mucopurulent, greenish or yellowish. In seven of the ten cases, it was bloody or streaked with blood.

In the acute cases, the onset was sudden with chills, fever and evidence of acute bronchitis with headache, rheumatoid pains, leaving marked weakness for five months, and cough with expectoration, sometimes streaked with blood. In the first acute case, the patient without warning began to cough up blood—about a glass and one-half, then there was a calm for thirty-five days.

during which there was scarcely any cough, then a fresh hemoptysis. The other patient with an acute attack, had chills, fever, slight cough and pain under the right nipple; there were also signs of dry pleuritis: hemoptysis followed twenty-five days later.

Temperature in the chronic cases was habitually normal, sometimes a little above. In the acute cases, it oscillated between  $99.5^{\circ}$  F. and  $102.2^{\circ}$  F., but never lasted over ten days.

Physical examination nearly always revealed redness of the throat, with folliculitis and adherent false membranes, yellowish or dirty brown in color, leading to the suspicion that the pharynx as well had been invaded. Nothing could be found in the chest, as a rule.

The method of contagion is still unknown. As a result of his observations, Farah believes the contagion is not

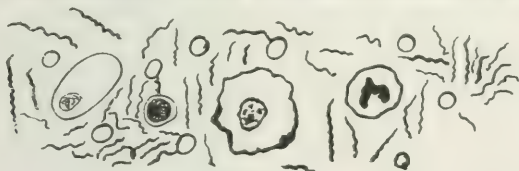


Fig. 6. Bronchial spirochetosis (Castellani).

so great as has been claimed, none of the patients transmitted the disease to their families, notwithstanding the crowded dwellings.

All the cases seen by Farah had been mistaken for tuberculosis, especially if there had been hemoptysis. Examination of the sputum, however, showed the total absence of the tubercle bacillus in all, and the constant occurrence of Castellani's spirochete. Branch refers to a case in which both were found, but none of this type were encountered by Farah. Such examinations also allow differentiation from endemic hemoptysis by absence of *Distoma westermani*; from mycelial bronchitis by freedom from moulds; from influenza by absence of Pfeiffer's bacillus.

Prognosis *quoad vitam* is good, but there is a great tendency for the disease to become chronic. Patients apparently well often have recurrences in weeks, months or, as in one case, years after.

As regards treatment, in addition to the usual hygienic and dietetic measures, tartar emetic and arsenic (principally arsenobenzol) have often been successfully employed.

Farah in every case used intramuscular injections of iodine. This therapeusis was based on the fact that fowls after injections of iodine do not contract the form of spirochetosis common to them when bitten by ticks.

The preparation used was lipoidol, analogous to iodipin, and containing 54 per cent. of pure iodine in poppy-seed oil. Injections are almost or quite painless. A series of daily injections of 2 c.c. was given for from five to ten days, this was followed by from ten to twenty more injections every two or three days according to the individual tolerance. The second series was to assure death of the spirochetes. The sites selected for the injections were the muscles of the buttocks, and except for occasional dryness of the throat and nose there was no evidence of iodism. In patients with hemoptysis, calcium chloride was given internally at the same time.

The mouth and throat were carefully looked after. The former was kept clean, and the throat gargled every three days with a mixture of iodine, 1 part, iodide of potash, 1 part, and glycerine, 30 parts. Tonics, *c. g.*, Fellows' syrup, were occasionally prescribed.

Practically every patient was cured by this plan, as shown by the improvement in general condition, and disappearance of cough. In general relief was obtained after the first injection. The sputum was always examined again after the fifth injection, and the spirochetes found very rare, compared with the former abundance. When the second series of injections was completed, the organisms were practically absent, and coughing had stopped. Farah believes that the iodine has a direct bactericidal effect on the organisms themselves. Since starting this treatment, May, 1918, he has had no relapse.



## DISEASES OF THE LUNGS AND PLEURAE

### Pulmonary Infection with *Ascaris Lumbricoides*.

This description of a newly recognized cause of pulmonary disease—*ascaris lumbricoides*, comes from B. H. Ransom,<sup>3</sup> Chief of the Zoölogical Division, United States Bureau of Animal Industry, and is of decided interest to the physician.

It has been known for a long time that the common round worm of man, *Ascaris lumbricoides*, and the closely related and probably identical parasite of the pig (*Ascarus suum*) sometimes occur aberrantly in organs other than the small intestine, their usual location.

Until the recent investigation of Stewart, however, the fact that *ascaris* is regularly parasitic in the lungs during the early stage of its development, was not even suspected. Stewart's experiments were repeated by Yoshida and by Foster and the present author, and his important discovery that the larvae of *ascarus* after hatching in the intestines of an animal that swallows the egg, migrates to the lungs and then returns to the intestine, was fully confirmed.

Briefly, the course of development is as follows: The eggs pass out of the intestine of an infected animal (man or pig) in the feces. The eggs are not infective until the contained embryos develop to a vermiform stage, which requires a period of two weeks or more, according to the temperature of the surrounding medium, oxygen supply, and moisture. Accidentally, the embryos may hatch outside the body: but in this case they quickly perish. Within the highly impermeable egg shell, however, the fully developed embryo is very resistant to cold, dryness and other unfavorable conditions, and may remain alive for long periods of time, five years and possibly longer. If swallowed by some mammal, the eggs that contain fully developed embryos hatch in the small intestine. They will also hatch if artificially introduced beneath the skin.

(3) Jour. Amer. Med. Ass'n, Oct. 18, 1919.

Unless accidentally carried out of the body in the feces, the newly hatched larvae leave the lumen of the intestine and migrate to the liver, though some possibly go more directly to the heart, in both cases apparently aided by the circulation. From the liver, where they remain in most cases only a few days, they migrate to the lungs evidently by way of the hepatic veins, inferior vena cava, heart and pulmonary arteries. They are stopped in the lungs, by the capillaries, enter the air vesicles and bronchioles, pass up the bronchi and trachea, then into the esophagus, and finally reach the small intestine, where, if the animal infested is a suitable host, they establish themselves and continue their development to maturity. Occasionally some of the larvae appear to return to the heart from the lungs, as they may sometimes be found in the spleen, under the peritoneum of the abdominal cavity, and in other locations that they could scarcely reach except in the systemic circulation. In such locations they may attain the same stage of development that is reached by those in the lungs but it seems unlikely that they can succeed in regaining the intestine or in continuing their development.

The fact that ascaris in the course of its development regularly passes through the liver and lungs, naturally raises the question as to the damage it may do during its migration. Under experimental conditions it has been found that the migrating larvae may seriously injure the lungs. By analogy it is reasonable to suppose that ascaris may occasionally, if not frequently be involved in the production of pulmonary disease among human beings, especially young children. Young children are known to be more susceptible to infections with ascaris than older persons, just as young pigs are more susceptible than older pigs, and it may be presumed that children resemble young pigs also in being more liable to suffer from ascaris pneumonia than older persons. It is known that over fifty years ago a German physician, Mosler, fed ascaris eggs in numbers as large as several dozens to healthy children of various ages. In no instance did the children afterward pass worms following anthelmintic treatment, but in some cases it was

observed that the children a few days after the eggs were given to them suffered from fever and difficulty in breathing. In the light of our present knowledge, it is altogether likely that the symptoms in question were produced by an invasion of the lungs by ascaris larvae.

The facts brought out in this investigation are summarized by Ransom as follows:

Infection occurs as the result of swallowing eggs of the parasite containing fully developed embryos, no intermediate host being necessary.

After the young worms hatch in the intestine they do not immediately settle down, but migrate to the liver, lungs and other organs, meanwhile undergoing considerable growth and development.

Those that reach the lungs return to the intestine by way of the trachea and esophagus, then settle down and develop to maturity if in a suitable host (man, pig); otherwise they are soon eliminated in the feces (rat, mouse, guinea-pig, rabbit), or in some hosts (sheep, goat) may undergo an abortive development that falls short of fertile maturity.

Pneumonia commonly occurs in experimentally infected animals in from a week to ten days after infection, at a time when the invasion of the lungs by the migrating larvae is at its height.

**Pathology of Mustard Gas Inhalation.** From the Base Laboratory, Hospital Center, Allerey, Saone et Loire, France, there comes a report of pathology of mustard gas inhalation presented by G. W. Covey and M. Barron.<sup>3</sup>

Of the thirty-seven cases included in this study, thirty-five according to the field medical cards were due to mustard gas, one to mustard gas and phosgene, and one to phosgene alone. In thirty-four cases, the action of the gas on the respiratory tract was the main factor in causing death.

In describing the condition the authors say that the respiratory tract is attacked from the tip of the epiglottis to the terminal bronchioles and air vesicles. The effects seen here are due (1) to the intense irritation and escharotic action of the gas, and (2) to secondary infec-

(3) Amer. Jour. Med. Sci., June, 1919.

tion, which promptly occurs. As seen in the autopsy room, more or less of the entire mucosa over this region is covered by a fibrinopurulent exudate, a false membrane, from dirty-gray to yellowish or greenish-yellow in color depending somewhat on the amount of suppuration and blood pigments present. In many cases it covers the entire area from the tip of the epiglottis downward; in others it is in patches; and in relatively few does it cover the wall of the lower part of the pharynx.

The appearance of this membrane, both grossly and microscopically, is very similar to that usually seen in diphtheria. In addition, the clinical features are not unlike those in the laryngeal type of this disease.

In nearly all cases the larynx is attacked. Here the false membrane extends down into all the irregularities of this region.

In the trachea and larger bronchi, much the same pathology exists.

The lungs are usually very voluminous, due to a marked emphysema largely vesicular, but occasionally interstitial or bullous. Subpleural hemorrhages are frequent. There may or may not be a pleurisy depending on the extent of the secondary infection present.

In the older and more advanced cases necrosis is frequently present in the consolidated areas, and this becomes the more prominent feature.

Microscopically, the membranous exudate lining the lumen is exactly similar to that seen in diphtheria, consisting of masses of fibrin fixed with occasional leukocytes, cellular debris and plasma. This exudate extends down into the bronchioles, where at times the lumina are completely plugged.

The histologic picture varies, depending on the rapidity of death after injury and, consequently, on the dose and concentration of the inspired gas. In several cases that came to autopsy the dose was evidently overwhelming, resulting in death from the escharotic and irritating action alone.

In studying the bronchial tree, a marked feature found was the injection of the blood-vessels. In many of the

PLATE X.



Larynx and trachea two months and ten days after gassing. Note extensive ulcerations, most marked at the bifurcation. The large transversely placed ulcer in the lower part of the trachea perforated through a cartilaginous ring.—Covey and Barron, page 287.



PLATE XI.



Lung from same case as Plate X. (The trachea and larynx are lying back of the lung, with the epiglottis and base of tongue showing just beneath the base of lung). Note the numerous areas of consolidation scattered throughout the cut surfaces. In the centers of many of these the emptied lumina of the bronchioles may be seen. Note the ragged areas of necrosis and abscess cavities.—Covey and Barron, page 287.

PLATE XII.



Larynx and trachea from a case of mustard gas inhalation. Note extensive edema of aryepiglottic folds especially the right; thick, shaggy membrane covering the larynx and vocal cords; membrane in patches on the wall of the trachea and bronchi; small ulceration of the wall near the bifurcation.—Covey and Barron, page 287.



bronchial walls the enormously dilated capillaries present a picture of a capillary hemangioma.

The histology of the peripheral portion of the lungs shows little except vesicular emphysema. In later stages with advanced pneumonic involvement pleurisy may be present.

In the older cases, that is in patients who died of the secondary infection, rather than from the direct effect of the gas, there is a picture of bronchopneumonia.

No changes were evident in the bronchial walls that could be taken for bronchiectasis.

Detailed reports of the clinical conditions of four patients who died and came to autopsy, and accurate descriptions of the autopsy findings are presented.

In the accompanying illustrations (plates X to XII) are shown some of the conditions found at autopsy.

In a summary of the conditions which are found in these patients, the authors state that stage one, as represented in the first two cases, is characterized by mild edema, hemorrhage, beginning ulceration, early fibrinous deposit, emphysema and very early bronchopneumonia. The second stage is characterized by a marked fibrino-purulent pseudo-membrane, more extensive ulceration, emphysema, advanced bronchopneumonia and beginning necrosis. The third stage is marked by ulceration, necrosis and abscess formation, with massive bronchopneumonia. The attempts at healing are revealed by the organization and fibrosis.

#### **The Margin of Safety in the Pulmonary Circulation.**

A study of the factor of safety in the pulmonary circulation has led J. P. Simonds,<sup>4</sup> of the Northwestern University Medical School, Chicago, to carry out numerous experiments to determine the minimum amount of lung substance compatible with life. A number of dogs were injected with a suspension of bismuth subnitrate in olive oil. The systolic pressure was taken from the carotid artery and the oil-bismuth mixture was injected through a cannula in the femoral vein and washed in with a few cubic centimeters of physiologic salt solution.

In all these experiments the animals were under ether anesthesia.

(4) Amer. Jour. Med. Sci., April, 1919.

It was found that there are two elements in the factor of safety in the pulmonary circulation. The primary element has to do with the pulmonary vessels themselves. In the first place there is evidence that under normal conditions, there is present in the lungs a considerable amount of "dead vascular space" in which the vessels are more or less collapsed, or in which the blood does not actively circulate. Also, a most important consideration is that the vessels of the lungs very readily undergo passive dilatation. Their walls are relatively thin and the capillaries in the alveolar walls have little support. The existence of vasomotors in the lungs, as Howell has shown, has not been demonstrated. The pressure in the pulmonary artery is relatively low, the observed average pressure for dogs collected from the literature by Tigerstedt ranging from 16.9 to 29.6 mm. of mercury. Hence, the dilatation of these vessels is probably purely passive, and is dependent on the volume of blood in the lungs with or without increased pressure in the pulmonary artery.

The secondary element in the factor of safety is the readiness with which the right ventricle is able to increase its work and even to hypertrophy when necessary. It may be stated, as a general rule, that any obstruction in the pulmonary circulation of sufficient degree to raise the pressure in the pulmonary artery and of sufficient duration will result in hypertrophy of the right ventricle.

A blocking of any considerable portion of the vascular area of the lungs results, therefore, in an opening up of a part or all of the "dead vascular space;" also, to passive dilatation of the still patent vessels, especially of the capillaries and, further, to an increased pressure in the pulmonary arteries due to increased energy of the contractions of the right ventricle. As a result of the action of one or all of these elements, the amount of blood which reaches the left ventricle is not diminished until the obstruction reaches excessive proportions. It is conceivable, however, that the sudden occlusion of a very large proportion of the vascular area of the lungs, as when a large embolus plugs one of the primary branches



of the pulmonary artery, may cause the adaptive mechanism to break down and death to ensue rapidly.

The factor of safety in the pulmonary circulation may have a very practical importance in several ways:

It may act as a safety-valve to relieve back-pressure in diseases of the left side of the heart. It is thus an essential element in compensation in cardiac diseases. Kuno showed that the blood content of the lungs may vary from 8.8 per cent. to 19.44 per cent. of the total amount of blood in the body. The amount of blood that can be passively stored in the lungs and thus shunted from the general circulation may be as great as 120 per cent. of that normally present in those organs.

There is a close relation between the condition of the pulmonary capillaries and the ventilating capacity of the lungs. Peabody has shown that the "pulmonary reserve," that is, the relation between the minute volume of air breathed at rest and the highest minute volume which the patient is capable of breathing, is reduced in many cases of cardiac disease. This decreased capacity to breathe deeply may depend upon a change in the elasticity of the lungs which results from an engorgement of the pulmonary vessels. This is in accord with the observation that dyspnea is an earlier manifestation in mitral than in aortic lesions.

The factor of safety is responsible for the maintenance of normal systemic blood-pressure in those diseases of the lungs, such as emphysema, chronic interstitial pneumonia, lobar pneumonia and tuberculosis, in which there is an extensive reduction of the total vascular area of the lungs either by destruction or occlusion of large numbers of blood-vessels. It is in cases of this type that the secondary element—namely, increased activity or hypertrophy of the right ventricle—plays an important rôle; for in practically all the chronic diseases mentioned above there is some hypertrophy of the right ventricle.

This accounts, also, for the difficulty encountered by Mann and others in their attempts to produce fatal experimental pulmonary embolism, and for the relative rarity of fatal results in humans following the lodgment of aseptic emboli in the lungs.

**Paratyphoid Infections of the Pleura.** Pneumonia, and bronchitis, especially the latter, are not uncommon complications of paratyphoid fever, but serofibrinous or purulent pleurisy due to infection with paratyphoid bacilli is apparently rare; and so rare that J. H. Abram and E. Glynn<sup>5</sup> present the records of two cases.

The first patient was a man, 38 years old, who was admitted to the hospital after being crushed between a wagon and a wall. The left side was strapped. During the eleven days he was in the surgical ward he had some diarrhea and typhoid fever was suspected. The man was then transferred to a medical ward with signs of consolidation at the left base. As the breath sounds were very feeble, although there was no displacement of the heart, a needle was inserted into the pleura and 5 c.cm. of slightly turbid fluid were obtained. From this fluid the paratyphoid bacillus was isolated and identified.

The second patient was a woman, 24 years old, who stated that three months previously she had suffered from influenza, and recently had had pain the left side. There were obvious signs of pleural effusion when she was admitted to the hospital. Pus was found in the chest on this side, and the empyema drained surgically. The patient made an uninterrupted recovery. In cultures of the pus paratyphoid bacilli *B.* were found.

Reference is made to numerous other cases similar to these that have been reported in the military service during the war.

**The Treatment of Empyema.** The treatment of empyema as carried out at Camp Mills, with special reference to the Philips empyema apparatus, is discussed by H. B. Philips, A. G. Langmann and C. L. Mix.<sup>6</sup>

By way of introduction, they state that the successful treatment of empyema depends on the recognition of the basic pathology of the condition. In the treatment of a collection of pus elsewhere in the body, simple incision and the establishment and maintenance of adequate drainage suffices in most cases to effect a cure. But in the chest cavity a different condition exists. When the pleural sac is opened for the drainage of pus,

(5) Lancet, Aug. 16, 1919.

(6) Jour. Amer. Med. Ass'n, May 3, 1919.

the normal negative pressure is immediately changed at atmospheric pressure (15 pounds to the square inch), the elastic lung collapses, the respiratory and circulatory embarrassment of the patient is increased instead of lessened, and a condition results which is the very thing to be avoided. To put it in the simplest form, it is adding a complication instead of ameliorating or aiding the condition. The indications for the most suc-

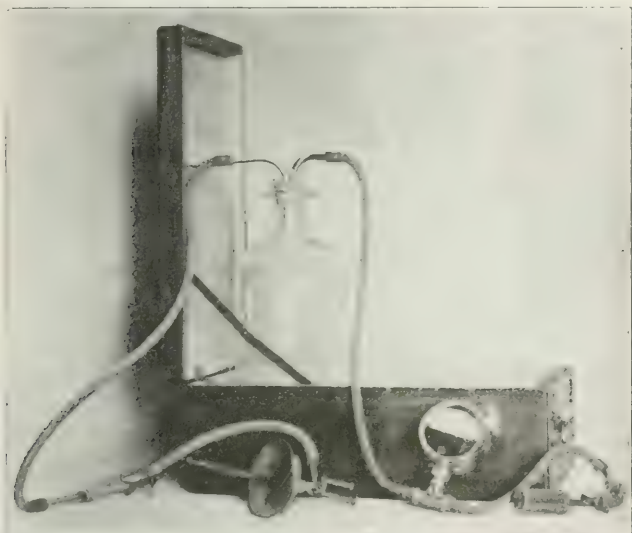


Fig. 7. Completely assembled apparatus with curet projecting from cannula orifice.

cessful treatment of this condition are obvious: the establishment of adequate drainage coincident with the exclusion of atmospheric pressure.

The Philips apparatus has been described in a previous report, but a brief summary of it is given here.

The apparatus consists of a special cannula, a bottle, a negative pressure manometer, a suction pump, and connecting rubber tubing. The cannula is of special design so as to be used for a trocar cannula for the thoracotomy and, being also non-obstructible, it remains in the chest wall until the empyema sac has been obliterated.

A rubber suction cap surrounds the cannula, and permits of an absolutely air-tight connection with the pleural sac (Fig. 7). This makes it possible to empty the pleural sac with non-obstructible drainage, maintaining a continuous negative pressure of from 30 to 60 mm. of mercury until the empyema sac has been obliterated and firm adhesions have formed between the visceral and parietal pleurae, when the apparatus may be removed.

The patients treated are divided into four groups as follows:

1. Those treated by simple repeated aspirations.
2. Those treated by intercostal drainage.
3. Those treated by rib-resection drainage.
4. Those treated with the Philips apparatus.

Experience led the authors to feel that the contraindications for repeated aspirations were as follows:

The character of the exudate such that it obstructs the cannula or needle.

Absence of improvement following this treatment.

The appearance of a complicating pneumothorax following aspirations.

Severe toxemia of the patient.

In the second group there were ten cases. Among these, two complete cures were effected in about six weeks' time. There was a mortality of 30 per cent., none of the cases being complicated by coincident active pneumonia. Pneumothorax could not be excluded by this method of treatment and to all appearances the drainage was not adequate. This method consisted of intercostal drainage.

Twelve patients were treated by rib-resection drainage. The authors state that the impression from this group of cases makes one feel that the postponement of the operation gives the patient an easier time, with apparently less risk at the operation. However, it appears to be an advantage paid for in convalescent time, for undoubtedly the delay permits the formation of adhesions in a partially collapsed lung, which enhances the chronicity of the condition.

Sixteen patients were treated with the Philips apparatus, and from the results obtained with this group it is stated that complete expansion of the lung was se-

cured in an average of three days after the application of the apparatus.

The mortality of straightforward cases of empyema, that is, those not complicated by coincident active pneumonia, was *nil*.

A large pneumothorax is exceedingly improbable (not encountered in this experience); and the open pneumothorax in all its dangers, so thoroughly and carefully considered and cautioned against by Graham and Bell, is impossible after the apparatus has been applied only a few days, for by this time the lung has been very considerably expanded, and a good part of it has become adherent to the chest wall in its expanded condition.

The duration of empyema as such is very materially shortened, by this method.

These experiences lead the authors to state that repeated aspiration as a curative procedure is not feasible in most instances. As a palliative procedure it permits of the formation of a pneumothorax in most cases, and its value is therefore questionable. Severe toxemia is a contraindication in repeated aspiration treatment. Intercostal drainage is impossible, in the experience of these workers, without the production of a complicating pneumothorax, and as it possesses the disadvantage without the advantages afforded by rib-resection, they feel that the latter is the operation of choice if the apparatus is not available.

Shock and cardiac respiratory embarrassment are minimized by the use of this apparatus.

It affords the most desirable method of treatment in any stage of the empyema, because there is exclusion of atmospheric pressure, secondary infection is excluded, the necessity for operation is done away with entirely, the duration both of the condition and the treatment are very materially shortened, and it is a clean, simple, sanitary and economical method of getting rid of the pus.

Open pneumothorax is absolutely prevented by the use of this apparatus.

**Management of Postpneumonic Empyema.** This paper is based upon the management of 310 patients who developed empyema among approximately 4000 patients with pneumonia at Fort Riley, Kansas. The report



is made by W. J. Stone,<sup>7</sup> of Toledo, Ohio, who includes in it only those cases which required treatment by aspiration or operation. There were available for this report thirty-five empyema patients who recovered by repeated aspirations alone, while 275 came to operation.

Because of the interest attached to variations of treatment, with increasing experience, these empyema patients have been grouped, depending largely on three-time intervals, as follows:

1. First Series: Early operation (Oct. 20, 1917, to Jan. 21, 1918) eighty-five cases. Mortality 61.2 per cent.

2. Second Series: Early aspirations and late operation (Jan. 12, 1918, to Aug. 10, 1918), ninety-six cases. Mortality, 15.6 per cent.

3. Third Series: Early aspirations and late operation (Oct. 18, 1918, to Feb. 14, 1919), ninety-four cases. Mortality, 9.5 per cent.

The three series of operated empyemas are comparable as to number. Each series represents as accurately as possible, but with some overlapping, different types of preceding pneumonia. The series are also comparable as a type of infection.

The first series of eighty-five patients occurred during the measles epidemic, which affected the 89th and 92nd Divisions of the Army, stationed at Camp Funston.

A comparison of the types of infection in the three series of empyema is made in the following table:

		Streptococcus	Pneumococcus
	Number	per cent.	per cent.
First series .....	71	73.2	26.7
Second series .....	95	73.6	26.3
Third series .....	85	70.4	29.4

Comparative recoveries in this type of infection in the three series are shown by the following figures:

		Streptococcus	Pneumococcus
	Number	recoveries per cent.	recoveries per cent.
First series .....	71	36.5	47.4
Second series .....	95	82.6	87.5
Third series .....	85	93.3	84.0

(7) Amer. Jour. Med. Sci., July, 1919.

Of the complications observed subsequent to operation, nephritis was found at necropsy in 85.7 per cent or twenty-one patients, who died subsequent to the operations of the second and third series. In a considerable number of these patients scarlet fever had immediately preceded the pneumonia and empyema.

Pericarditis, seropurulent or purulent, occurred in 36 per cent. of forty-eight patients who came to necropsy subsequent to empyema operation. It occurred in 46 per cent. of 100 patients with non-operated empyema who came to necropsy.

The occurrence of substernal pus pockets varied with the type of pneumonia. It was more commonly noted subsequent to the type of interstitial pneumonia which followed measles and the empyema constituting the first series of operations, 18.5 per cent. of twenty-seven necropsies. It also was encountered in 14.3 per cent. of the instances of empyema necropsies of the second series, which likewise occurred subsequent to an epidemic of streptococcus pneumonia, in which many interstitial types of pneumonia were encountered. In the third series of empyema necropsies following influenzal pneumonia, this complication was not encountered and but few instances of the interstitial types of pneumonia occurred.

Peritonitis, serofibrinous or purulent diffuse, was seen in fourteen of the forty-eight necropsies (29.2 per cent.) constituting the patients with operated empyema in the series.

Bilateral empyema was found in eleven, or 22.9 per cent., of forty-eight patients who came to necropsy in the three series of empyema operations.

Bilateral pneumonia was found in fifteen or 31.2 per cent. of forty-eight patients who came to necropsy in the three series of empyema operations. In this same group of necropsies abscess of the lungs was found in seven, or 41.6 per cent. In five, or 71.4 per cent. the abscesses were multiple and occurred on the affected side.

Other complications: Less frequent conditions found at necropsy in the three series of empyema operations were tuberculosis, pulmonary fibrocaseous or miliary:

metastatic meningitis; endocarditis; hydropericardium; embolism and thrombosis of mesenteric vessels; and myocardial degeneration. The myocardial softening differed in no essential particular from that degree of

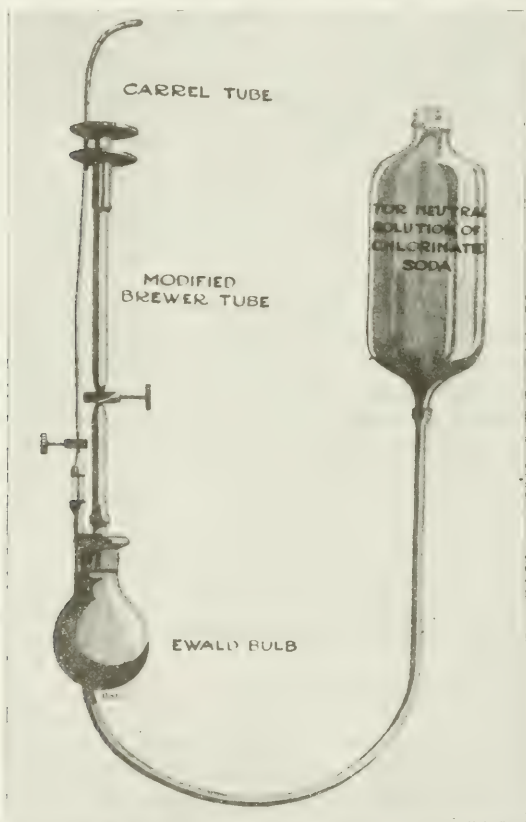


Fig. 8. Apparatus for continuous or interrupted empyema irrigation and suction as used at U. S. Army Base Hospital, Fort Riley, Kansas.

parenchymatous degeneration affecting all organs in the presence of a chronic septic process. Ascites as a result of myocardial degeneration and nephritis occurred in one instance.

Under the heading of treatment, Stone says that in performing repeated aspirations, one must expect the fever, pulse-rate and many times the respiratory embarrassment to diminish. In the present work the author and his associates were guided by four points in deciding on the proper time for operation in a unilateral empyema: First, the quantity and character of the pus,



Fig. 9. Apparatus in position for irrigation and suction in empyema.

second, the type of infection, third, the presence or absence of complications, and fourth, the length of time necessary to show improvement in the general condition of the patient under the aspiration.

Tabulated results show that an average of six aspirations was performed and that the average was about nineteen days before operation for the patients of the second series; also, that the average number of aspira-

tions was 3.7, and that the interval before operation was 13.5 days for the patients of the third series. The time for operation will, in general, depend on the four factors mentioned above. Five aspirations during a period of from twelve to fourteen days if the patient has shown improvement will constitute an average. Operation may with greater safety be longer postponed on a patient with pneumococcus than on one with streptococcus infection.

In performing the aspirations, when the pus was thick and because of some complications, such as an active pneumonia on the opposite side or a bilateral empyema, operation did not at the time appear advisable, intrapleural lavage, using sterile saline solution, was performed at the time of aspiration in order to dilute the pus and permit of its aspiration.

In this manner quantities of pus varying in amounts from 400 to 800 c.c. could be removed in excess of the amount secured by the first aspiration and in excess of the amount of saline solution introduced.

At the time of operation, the patient received hypodermically  $\frac{1}{8}$  grain of morphine and  $\frac{1}{200}$  grain of hyoscine one hour before going to the operating room. This was repeated one half hour before the operation, except in markedly weakened patients. General ether anesthesia has been proved safe for these patients in the absence of an active pneumonic process and in individuals upon whom a number of aspirations have been performed. This was especially true if after the ether anesthetic the lungs were thoroughly ventilated of ether vapor by oxygen inhalation with the closed cone for about five minutes. Recovery from the anesthetic occurred rapidly and no ill effects from the ether were evident subsequently.

The attempt was made at the time to secure copious drainage for the first forty-eight hours by means of a single large drainage tube (about 4 inches long and  $3\frac{1}{4}$  inch diameter), after which, in many patients, the modified Brewer tube, with Ewald suction bulb and Carrell tube for irrigation shown in Figure 8 was inserted. The skin opening should be much longer (about two inches) than the width of the flange on the Brewer tube.



While this small incision made it more difficult for the operator to resect one inch of rib, it was possible to fit the Brewer tube tighter, and better negative pressure by the suction of the Ewald bulb could be secured. At the present time, no irrigation is used for the first forty-eight hours. At the end of that period irrigation is carried out by means of the apparatus, as shown in Figure 9. Neutral solution of chlorinated soda in quantities of from 100 to 300 c.c., depending upon the size of the cavity, was allowed to flow in or was injected by means of a hand syringe every two hours. Suction was secured at the end of two hours to remove the solution and pus before the fresh solution was placed in the cavity. At the end of the first week, suction was more or less continuously employed and one daily irrigation in the dressing room substituted for the continuous irrigation in the wards. Pain contraindicated suction. Irrigation with the neutral solution of chlorinated soda was contraindicated if a communication with a bronchus was suspected. It has not been necessary to have any extensive secondary operation performed for large open pneumothorax or cavity in any of these patients, although sequestrectomy for a small portion of necrotic rib and dissection of the sinus was necessary in a few patients.

The daily irrigations were, as a rule, continued until pus was absent. The Brewer tube was removed after two weeks and gradually decreasing sizes of plain rubber tubing substituted for drainage purposes. The count of the number of bacterial cells per field from smears of the discharge as an index to the efficiency of the irrigation has given in Stone's hands no more definite information as to the safe time for closure of these wounds than the clinical evidence. The ability of the lung on the affected side to expand determined to large degree the extent of drainage and the obliteration of the empyema cavity. Posture in bed and suction assisted drainage but drainage was greatly facilitated if expansion of the lung could occur. The external opening should therefore be decreased in size as rapidly as possible by substituting smaller-sized tubes sufficiently large for drainage and irrigation.

The postoperative dressings required rigid surgical cleanliness to prevent secondary infection of the pleura, a condition particularly liable to occur. A high calorie diet was used to make up for the extensive tissue waste which accompanied the chronic sepsis. A diet of 3500 to 4000 calories could be readily secured by augmenting the regular or special diet with carbohydrates and fats.

**Study of Hemolytic Streptococci in the Throat in Empyema.** This study was carried out by B. Lucke and M. H. Ray,<sup>8</sup> in the winter of 1917 and 1918 at Camp Zachary Taylor.

During this time infections with hemolytic streptococci formed one of the most serious medical problems at this as well as at other army camps. At first, this infection was intercurrent with measles, later, it seemed to constitute an independent epidemic. The respiratory and auditory tracts were chiefly involved, the lesions being sore throat, bronchopneumonia frequently complicated by empyema, pericarditis and peritonitis, and otitis and mastoiditis occasionally complicated by meningitis. Of these various infections, bronchopneumonia was the most important, especially since in over 30 per cent. of cases it was accompanied by empyema.

The purpose of this study was to ascertain whether the streptococci from such various sources were biologically similar or dissimilar, and whether they were identical with strains isolated from empyema fluids. It has been shown by Kinsella that all hemolytic streptococci are immunologically identical in the complement-fixation test.

Further to study their relationship, the following criteria have been employed in the present work: Growth in serum peptone broth, morphology, hemolysin production on blood agar, quantitative hemolysin estimation, carbohydrate reaction and virulence for rats.

The material obtained for this work consisted of organisms isolated from the throats of patients belonging to five disease groups: First, acute infections of the upper respiratory tract; second, non-infectious diseases from apparently normal throats; third, uncomplicated measles; fourth, from the pus of patients suffering from

(8) Jour. Inf. Dis., June, 1919.

empyema preceded by measles, and fifth, empyema not preceded by measles.

No difficulty was encountered in isolating streptococci in pure cultures because of their general occurrence. Throat swabbings on blood-agar plates often gave a pure culture and the pleural fluid contained in every instance a pure growth.

After isolation from the original material, cultures were repeatedly plated to insure their purity. It is noteworthy here that smears from pleural fluid showed such a dense growth of short and long chains of streptococci as to resemble the growth in artificial culture mediums. In several instances, the empyema patients received treatment with gentian-violet irrigation. The work done in association with the surgical department would seem to indicate that no profit was experienced by the patient with the use of gentian violet, and it was perfectly clear that this dye exerted no inhibitive action on the organisms in the pus, for smears and cultures from such cases presented no variations and the authors kept streptococci for several months in fluid heavily tinged with gentian violet.

A further description of technique and a tabulation of results and their discussion follows.

The conclusion reached is that streptococci isolated from the throat and from empyema exudates during the winter of 1917-18 appeared biologically identical and highly virulent as based on the criteria mentioned in the first part of this abstract. The study has confirmed the observation of others using immunologic procedures, and gives additional support to the belief that the streptococcus carrier state is an indication of the possibility of complications in respiratory tract disease.

**Differential Diagnosis of Pulmonary Abscess, Bronchiectasis and Pulmonary Tuberculosis.** This article consists of a discussion of points on differential diagnostic value in pulmonary abscess, bronchiectasis, and pulmonary tuberculosis, with an explanation of the cause of the difference in auscultatory findings. It is presented by F. M. Pottenger,<sup>9</sup> who states that both pulmonary

(9) Amer. Jour. Med. Sci., October, 1919.

abscess and bronchiectasis are often diagnosed as tuberculosis on the basis of cough and expectoration.

The fact that bacilli are not found is no longer sufficient to prove the non-tuberculosis nature of a pulmonary process; consequently, this fact confuses more than it helps.

Concerning the clinical history, Pottenger points out that pulmonary abscess usually follows acute infection of the lungs. It also follows operations on the teeth, tonsils and nasal cavities now and then, the infectious material being aspirated into the lungs. This etiology the author considers to be more common after tonsil operations than is generally believed. Abscesses produced in this way furnish a history of acute onset. Expectoration is sometimes foul-smelling, usually profuse at first, varying in quantity later. There are periodical rises in temperature, sometimes bloody expectoration and clubbing of the fingers. This last symptom has been seen to come on as early as six weeks after the onset. Pulmonary abscess following influenza during the recent epidemic, has been a common experience among clinicians. The abscess is usually found in the lower half of the lung, and is often situated in fibrous tissue which has resulted from the infection.

Bronchiectasis usually follows pneumonia in childhood, although a few instances occur in adolescence and early adult life. The author has seen it rarely begin in those in middle life, unless it was of a tuberculous nature. The cough in patients in this condition is loose, indicating that the sputum is in the larger tubes where it is easily moved. The history of cough with expectoration following and persisting after a pneumonia in childhood is of itself nearly sufficient for the diagnosis of the post-pneumonic type. With this condition, the fingers are often clubbed, but this sign is not so important here as in pulmonary abscess. It is not so constant, nor does it appear so quickly.

In pulmonary tuberculosis, with cavity formation, with rare exceptions, an abscess cavity forms only after the disease has existed as a clinical entity for some time. Cavity formation in tuberculosis is more liable to be preceded by repeated attacks of toxemia, sometimes

months apart, while pulmonary abscess usually comes on promptly following an acute infection in a patient who was previously in good health. The patient with tuberculosis presents more of the symptoms of nerve irritability, and of nutritional disturbances when the acute process comes on than is seen in the conditions mentioned above. Repeated attacks of bronchitis are common in bronchiectasis and in tuberculosis, but not in pulmonary abscess.

Concerning the nature of pulmonary abscess, Pottinger says that it is a disease caused by microorganisms producing acute infection. Abscesses caused by these germs result from an extension of an infection in the respiratory tract, or from aspirated material during operations on the upper respiratory tract.

Bronchiectasis often follows fibrosis and contraction of the pulmonary tissues, and is commonly found near the hilum, although the infection may involve the bronchi in all parts of the lungs.

Pulmonary tuberculosis is not a disease which results immediately on the bacteria gaining access to the air passages. If the patient has been previously infected, the bacilli after entering the tissues pass readily to and settle in the lymphatic glands, and are later carried through the blood or lymph stream to be deposited in the capillaries or lymph spaces of the pulmonary tissue. Mechanical and chemical conditions that favor the development of pulmonary abscess are not favorable to the formation of tuberculous cavities. Consequently, active tuberculosis with cavity formation is usually first found near the apices, while pulmonary abscess is usually found in the lower lobes, and bronchiectasis may be found in any portion, but often affects the large bronchi near the hilum.

In making physical examinations, inspection reveals a diminution of motion, nearly always to be noted on the side of the involvement of all of these infections. In pulmonary tuberculosis this may be difficult to ascertain in those instances in which there is a lesion in both lungs. The mediastinum is shifted toward the affected side in all these conditions. By inspection and palpation there can be determined the reflex spasm in



the muscles, and degeneration of the soft tissues—skin, subcutaneous tissues and muscles, and these conditions, as a rule, are found not so much in pulmonary abscess and bronchiectasis as they are in pulmonary tuberculosis. The muscles of the shoulder girdle and diaphragm are more tense, the increased tension in the latter is in-

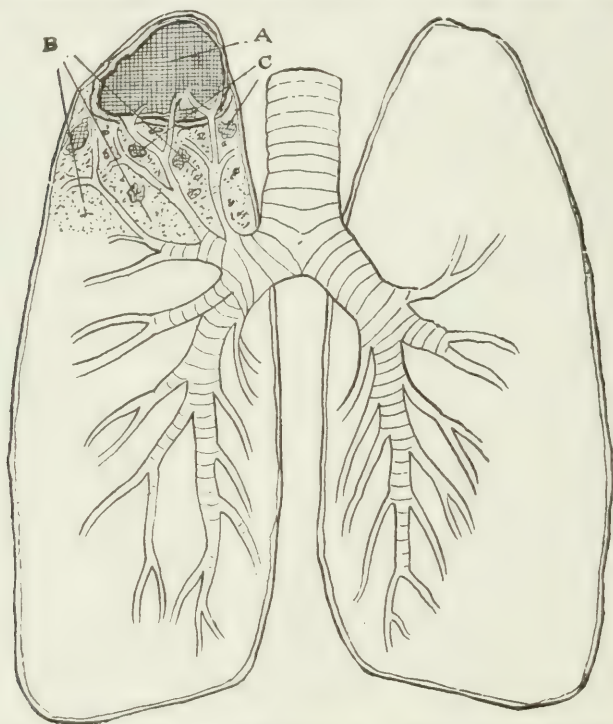


Fig. 10. Diagrammatic illustration of a cavity due to pulmonary tuberculosis. The cavity, A, is surrounded by tissue which is the seat of tuberculous infiltration, B, and which contains many small cavities, C. These are ideal conditions for the production of râles.

ferred from the limited motion, during the activity of the tuberculous process than is found in the other diseases considered. When the disease becomes chronic, these muscles and the soft structures (skin and subcutaneous tissue) in the neck and down to the second

rib anteriorly and the spine of the scapula posteriorly show far more reflex trophic changes in tuberculosis than in the other two diseases.

By auscultation, the signs elicited in pulmonary tuberculosis with expectoration are usually more or less

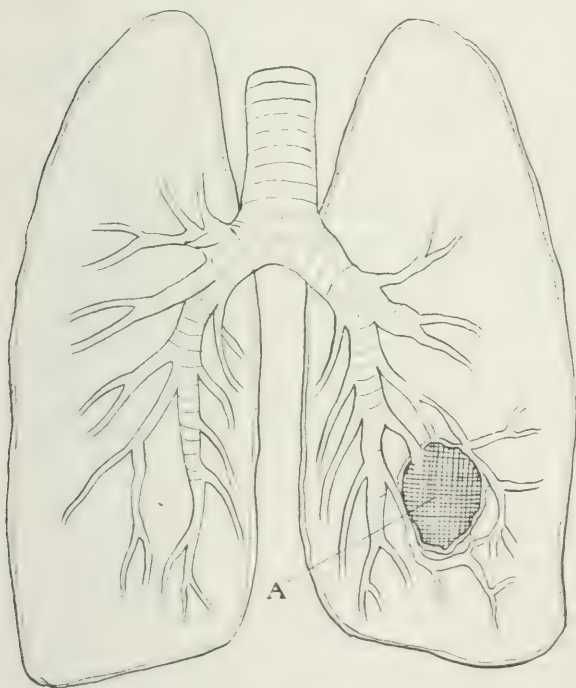


Fig. 11. Diagrammatic illustration of acute pulmonary abscess. The abscess, A, is situated in the midst of and surrounded by healthy pulmonary tissue. The source of rales is the cavity itself and the bronchi leading from it. This condition is not favorable to the production of many rales.

definite. If a cavity is present in active tuberculosis it is found in the midst of actively diseased tissue, if chronic, the tuberculous process outside the cavity may be partly or wholly healed, and the signs elicited on auscultation may be similar to those of pulmonary abscess. The signs of pulmonary abscess and of bron-

chiectasis as determined on auscultation are usually few and often very indefinite.

[In the stage of pulmonary abscess before drainage is established through the bronchi there may be entire absence of breath sounds and of râles in the infected area. A like absence of breath sounds may be found in obstructive bronchiectasis.—B.]

The relative prominence of râles in these three affections is illustrated in the accompanying illustrations (Figs. 10 and 11).

Figure 10 illustrates the conditions present in pulmonary tuberculosis. The large cavity "A" has formed near the apex. It will be noted that this has taken place in the area which is the seat of a widespread tuberculous involvement, as illustrated by the dotted area "B," throughout which there are numerous small cavities seen. Here are indicated the ideal conditions for the production of crepitation and mucus râles: inflammation with foci of necrosis involving the walls of air cells and bronchi accompanied by an occasional production of mucus which must find its way toward the trachea through the bronchi of all sizes. The cavity itself is at times the seat of coarse râles, at other times no râles are elicited over it.

Figure 11 illustrates the condition present in pulmonary abscess. An abscess "A" has formed as a result of a bacterial infection. As a rule, the first pulmonary abscess which forms is an acute process coming on within two days after the implantation of bacteria has occurred. The surrounding tissues may not be at all infected. This is particularly characteristic of those abscesses which follow operative procedure upon the respiratory tract. The abscess often forms in a single focus, just as a boil forms on the surface of the body. A pus-forming pocket remains which discharges through the bronchus. The conditions in the surrounding tissues which favor the production of crepitations and râles as shown in pulmonary tuberculosis in Figure 10, are absent, and the chief source of whatever râles may be present is the abscess cavity itself and the bronchus or bronchi which drain it. The result is that crepitations and mucus râles are few in abscesses produced by acute

infections as compared with the abscess cavities which accompany pulmonary tuberculosis unless the latter had existed for a long time and the tuberculous involvement of the surrounding tissues is healed. When multiple abscesses form in non-tuberculous lesions, each one repeats the same cycle of events as noted in the acute single abscess.

Much the same condition is found in bronchiectasis so far as the production of râles is concerned as has just been described in pulmonary abscess. The bronchi are dilated and their walls thickened in such a manner that their dilatations have much the same physical appearance as abscess cavities.

**Treatment of Serofibrinous Pleurisy by Artificial Pneumothorax.** In a communication on the treatment of serofibrinous pleurisy, Wiel<sup>10</sup> recommends the injection of air after the puncture of the chest for serofibrinous pleurisy. He considers that by the use of this method there is less danger of secondary complications and it also prevents adhesions. Of eighty-six cases of serofibrinous pleurisy subjected to puncture alone; seventy-two or 84 per cent. showed marked secondary trouble a few months later. In a second series of fifty cases in which puncture was followed by injection of air, in forty-one or 82 per cent. recovery ensued without adhesions. The remaining nine cases which showed adhesions, were cases of long-standing before treatment. Seventeen patients treated by this method recovered in from two to three months after a single pneumothorax and the patients each gained from ten to fifteen pounds. Thirty-three required more than one injection, but eventually recovered. In patients who present recurring accumulation of fluid, recovery is much delayed, but cure is possible with prolonged treatment. The author cites the case of a patient who received ten injections of air during a period of a year with ultimate cure.

The advantage claimed for this method is the treatment of those cases in which tuberculosis is the underlying cause of the pleural effusion, the effect of rest to the lungs and the arrest of the tuberculosis. The author controlled his treatment with the Roentgen ray and radioscope.

<sup>10</sup> Bull. de l'acad. de méd., June 24, 1919.

## DISEASES OF THE HEART AND BLOOD-VESSELS

**New Diagnostic Methods in Cardiac Disease.** The two diagnostic methods presented by J. E. Benjamin and E. R. Brooks<sup>1</sup> have to do with the diagnosis of tachycardia and mitral stenosis. The value of the first test lies in the fact that the separation of the more stubborn cases of simple tachycardia from the persistent type is facilitated.

The individual on direction drops the head and bends forward to about an angle of 45 degrees, whereupon the rapid heart will retard to a remarkable degree very quickly; sometimes to half the original rate, if the case is one of simple tachycardia. The other type is not affected at all. Also, in the former instance the rate in the bending position corresponds fairly accurately to the rate in the recumbent posture. It requires less time to resume a nearly normal rate in the former than in the latter procedure, and is thus a quicker method. The test was applied in a very large number of cases with gratifying results. A certain number of soldiers who responded to this test were followed up; they were found to be doing full duty.

Concerning mitral stenosis, the authors state that a probable explanation of the large number of cases of mitral stenosis reported from the various camps is the fact that the keen excitement and the influence of new environment caused the heart tones in many instances to become altered in character. They present the results of their observations in the use of amyl nitrite inhalations as an aid in this difficulty. The procedure was recommended in 1918 by R. A. Morison, who suggested, after a fair trial of this drug, that a valuable aid was at hand to eliminate the difficulty in the diagnosis of the existence or non-existence of presystolic murmur. The authors followed his method in each instance, ampules of amyl nitrite, containing 3 minims each, were employed. One ampule was used in each doubtful case.

(1) Jour. Amer. Med. Ass'n, March 8, 1919.



Of course, the influence on the heart so far as it concerns these experiments is very similar to the effect of exercise. However, there is this one great advantage. It is possible to listen to the heart during its period of increasing activity and acceleration and there is no attending dyspnea as a disturbing factor. In other words, as the patient administers the drug to himself the observer listens at the apex of the heart until the desired effect of the drug is produced. In this way several phases of increasing cardiac activity are observed. In all, forty-eight cases were examined, and it is the opinion of the observers that a very valuable aid in diagnosis has been obtained. In ten cases, the doubtful nature of the presystolic sound was intensified to such a degree as to admit of a positive diagnosis of mitral stenosis. In the balance of the cases, the suggestive presystolic sounds were eliminated. The greatest difficulty was experienced in the negro, for here the element of neurosis was clearly manifest and this influence on the heart produces, at times, varied changes. Chief among these are a greatly accentuated pulmonic second and a very loud sound at the apex and a thrill at this area, the timing of which is frequently difficult. In such cases recourse to inhalations as described above were found to be valuable.

**Test Marches and Functional Cardiac Aptitude in Tachycardia.** M. Leconte<sup>2</sup> remarks that the different tests proposed for determining this aptitude often give results according but little with the other clinical findings. He speculated whether by prolonging the transient effort exerted by such tests it might not be possible to obtain clearer results—the cardiac fatigue being less ephemeral, as well as less capricious, certain exogenous elements, *e. g.*, the neuropathic factor, thus losing their influence.

The test devised by him consisted of a walk of 10 kilometers, first on level, then on hilly ground, with a rest of ten minutes in each hour. Pulse and arterial pressure were taken at the start of the walk, also at the beginning, middle and end of the rest period and, finally, after return home, at several times during the next hour.

(2) *Archiv. d. mal. du cœur*, January, 1919.

Several "functional" cardiopaths were subjected to the test: In subjects who had tachycardia only occasionally, and in whom the other tests gave inconstant results, the acceleration observed was slight or rapidly subsided; the action on the arterial pressure was irregular. Those with habitual tachycardia reacted more markedly, the acceleration provoked was more evident and more lasting; the arterial tension, as a rule, remained unchanged, but once more there were discordant results.

The conclusion is that sphygmomanometric reactions are too uncertain to prove of value, the reactions above referred to are more regular than with the other tests, but even the test march does not give a fixed relation between the results obtained and the functional aptitude of the heart—it can only give additional clinical findings.

**The Clinical Value of the Electrocardiograph.** Because of the clearness with which the clinical value of the electrocardiograph is brought out by Joseph Sailer,<sup>3</sup> of the University of Pennsylvania School of Medicine, the greater part of this article is used.

While it is not plain that anything new is presented here, there is much that will aid the general practitioner in undersanding a method that is being used more and more every day in studying pathologic conditions of the heart.

The instrument consists essentially of a delicate platinum or gilded quartz wire, usually called the string, suspended between the poles of a powerful electromagnet. The string is one of the most delicate instruments known, its diameter being from 0.002 to 0.003 mm., that is 2 or 3, 25000th of an inch. The current from the heart passes through the string and causes it to deviate from side to side. The string is placed in the field of a microscope and its magnified shadow thrown through a narrow slit upon a photographic film. The shadow therefore moves from side to side, but as it is customary to hold the shadow lines horizontally the deviations are spoken of as being up or down. If the shadow deviates to the right, as one faces the plate, it causes an upward deflection, and if to the left a downward deflection. The instrument is so constructed that the upward deflection

(3) Jour. Med. Soc. New Jersey, October, 1919.

represents a current negative at the upper end of the string and positive at the lower end. The current passes through the body from one limb to another and then by means of pads and wires through the galvanometer. There are methods of neutralizing the skin resistance, of changing from one limb to another and of altering the resistance, but these have all to do with the technical handling of the instrument and only influence the reading of the curves when they have been improperly used.

Briefly, the contraction of the heart originates in a group of interlacing, pale, slender muscular fibers at the junction of the vena cava and the right auricle. The Kieth Flack or sino-auricular node originates the impulses which pass along a group of similar, but somewhat thicker fibers, the fibers of Purkinje, to the inter-auricular septum, where there is another interlacement, the node of Towara. Then a band passes downward toward the ventricles, the bundle of His, bifurcates, and the two bundles are distributed, first to the papillary muscles and ultimately to the muscles of the ventricles. These fibers apparently can induce contraction, can conduct the contraction impulse, and themselves contract. They represent, therefore, a less differentiated and more primitive type of tissue. Whether the primary impulse comes from the muscle tissue itself or from the ganglion cells placed around it, is still a subject for dispute.

According to the leads, as they are called, that is direction of the currents through the body, the picture produced by the deviation of the string varies. These leads may be various, but for convenience of comparison three have been adopted as standards, numbered I., II., and III. Lead I. is from the right to the left arm. Lead II. is from the right arm to the left leg. Lead III. is from the left arm to the left leg.

The electrocardiogram shows deviations of the string when the auricle and when the ventricle contract, named, respectively, the auricular and the ventricular complexes. These complexes are fairly constant in normal hearts with some variations that apparently do not denote abnormalities, and show certain very character-

istic deviations in abnormal hearts, that indicate the nature and, to some extent, the degree of abnormality.

The normal picture of Lead I. consists of a thick line produced by the fine vibrations of the string not transmitting a current. When the auricle contracts, as a result of the impulse of the pacemaker in the sino-auricular node, there is a slow deviation upward. The breadth of the base and the thickness of the line indicate how slow it is. It is known arbitrarily as the *P* wave. It is always upward in the normal heart. From 0.12 to 0.18 seconds later there is a very sharp, slight deflection downward, often practically imperceptible, known as the *Q* wave, the beginning of the ventricular systole, followed immediately by a high, sharp upward deflection, the *R* wave; the down stroke usually descends below the line and forms the *S* wave. There is then a pause and a slow, thick point above the line appears, the *T* wave, indicating the end of the ventricular systole, possibly the contraction of the aortic and pulmonary rings.

In the second lead the *S* wave is usually more pronounced, giving rise to a zigzag ventricular complex, not unlike the conventional representation of a flash of lightning. The *P* and *T* waves are the same. In the third lead the appearance is similar of the first, that is a high *R* and small *S*, but the *T* may be inverted without apparent clinical significance. There is much else to study, the *P-R* interval, the breadth of *R*, the character of *P*, the height of *R* and the depth of *S*, the rhythm or its lack.

Two interesting questions are presented by the electrocardiograph: First, what is its value in diagnosis? Second, what help does it give in explaining the nature of cardiac disorders?

In diagnosis, the greater value of the electrocardiograph is its ability to determine which side of the heart is doing the most work. This is called preponderance right or left. The reaction is, as a rule, extremely delicate. It is more pronounced after effort or even in the standing position, but usually neither is necessary. It is shown by an alteration in the *R* and *S* waves. If *R* is small and *S* large in the first lead and *R* large and *S*

small or absent in the third lead, it is assumed that the right side of the heart is over-acting. If *R* is large and *S* small or absent in the first lead, and *R* small and *S* large in the third lead, it is assumed that the left heart is over-acting. The height of *R* and the depth of *S* bear some relation to the degree of preponderance.

In a general way, right preponderance means mitral disease, left preponderance aortic disease, right preponderance is therefore more common in the young and in women, left preponderance from middle age onward and in men. But they mean more than this. In congenital heart disease the preponderance is usually right, although the physical signs may lead to any kind of a diagnosis. Left preponderance may suggest renal as well as cardiac trouble, or that very indefinite condition known as vascular hypertension. It is also found in aneurysm and syphilitic aortitis, and indeed is a valuable suggestive sign of syphilis in men. The other conditions in which the electrocardiograph helps are the arrhythmias and the defects in conduction. It is also of some value in watching the course of a case, and helping in prognosis.

Nearly all that is known about the arrhythmias is due to the polygraph and the electrocardiograph. They are:

First, sinus arrhythmia, in which the heart beat slows during inspiration; occurring chiefly in the young probably neural in origin and of no great clinical importance. It needs no instruments for its recognition.

Second, total arrhythmia or auricular fibrillation, called first nodal arrhythmia, is a condition in which small groups of muscle fibers in the auricles contract independently. Although the impulses from the auricles pass to the ventricles, the majority of them are ineffective, and the ventricle beats irregularly and, because of the immense number of impulses, rapidly. It is characterized on the polygraph by the absence of the *A* wave in the jugular and apex tracing, in the latter the *A* wave may be absent in normal apex tracings; and in the electrocardiogram by the appearance of numerous small waves in the tracing that have more or less the character of the *P* wave and are irregularly spaced. In both, the ventricular complex, the *C* in the polygraph



and *Q*, *R*, *S*, *T* in the electrocardiogram, is irregularly spaced and gives evidence of irregular force. The condition usually occurs in mitral disease. It means as a rule decompensation, but may exist for years without noticeable discomfort. It is one of the conditions in which digitalis is a specific.

Auricular flutter is a condition in which the auricle contracts rapidly, but only alternate or third impulses pass. The ventricular rate therefore is one-half or one-third that of the auricular. It can only be recognized by instruments, is rare, and, as in fibrillation, digitalis is a specific. Tachycardia, paroxysmal and simple, is described by its name. It is of interest that the former is due to a dislocation of the auricular pacemaker.

In many respects one of the most interesting abnormal conditions of the heart is known as heart-block. The term almost explains itself. There is a delay in conduction of the impulse to contract from the auricles to the ventricles and as this condition takes place through the bundle of His, it is in this particular structure that heart-block usually occurs. A blockage may occur in the main bundle and affect both ventricles or be limited to one bundle and then one ventricle will be chiefly affected, but the rate of contraction of that ventricle will be the same as the other side. The degree of blockage may vary from a slight prolongation of the *P*, *R* interval to a total dissociation in which the auricle and ventricle beat entirely independently and at very different rates. In normal hearts, apparently, the ventricles act to a certain extent as a brake on the auricular pacemaker, which when left to itself beats at about 140 a minute. When left to themselves the ventricles are capable of continuing to pulsate at the rate of about 35 a minute, but there is of course much variation in both of these rates.

Consequently in total dissociation one sees either upon the polygraph or the electrocardiograph a curious phenomenon, of a great number of *A* or *P* waves, while the *C* waves and ventricular complex come at irregular intervals and without any reference to auricular contractions. The auricular pacemaker maintains its rhythmicity. The ventricular pacemaker is not rhyth-

mic and therefore it is found that the larger waves occur at irregular intervals. Moreover the ventricular pacemaker deprived of its normal stimulus shows not only a marked change in its time, but also in its character and abnormal ventricular complexes follow.

This brings up another factor in the study of the electrocardiograph tracings. When the electric impulse from a piece of muscle that has been removed from the body of a frog is studied, it shows a diaphasic phenomenon, that is as the electric current travels along the muscle fibers, there is at first a negative and then a positive wave and as the waves travel from one pole to the other the result on the electrocardiograph is a high wave above the line and then a deep wave below the line. These waves moreover are not always uniform, but different forms are seen that have been shown by Lewis to correspond to different points of origin in the ventricular substance. Experimentally it has been possible to produce a variety of these waves which may and probably do correspond with the pathologic waves found in these cases.

Clinically, heart-block has long been known but not, until the advent of the electrocardiograph, in its lesser stages. It is known now that in addition to prolongation of the *P R* interval there are forms in which not all auricular impulse can travel through the bundle of His and in these cases a certain proportion of ventricular contractions fail to occur. Next in severity to the prolongation of the *P R* interval there is usually an occasional dropping out of the ventricular beat. Later, it may be that every other ventricular response fails and there occurs a 2-1 rhythm. Then it may be that response occurs only to the third auricular impulse and there is a 3-1 interval. After this, dissociation as a rule becomes irregular and in a short time, as the case progresses, total dissociation occurs. When this happens, there is usually decompensation and apparently from time to time there are considerable intervals during which effective ventricular contractions cease and the patient becomes unconscious, giving rise to typical Stokes-Adams syndrome. These periods of unconsciousness may last for several minutes during which time the pulse is im-

perceptible at the wrist and cardiac contractions cannot be heard with the stethoscope. The author has not observed any cases with the electrocardiograph during the attack, but with the polygraph it appears that the auricles continue to pulsate, at least the A wave in the jugular pulse can be obtained.

The treatment of heart-block, of course, depends first upon the removal of the cause. After this is removed the prognosis is not necessarily unfavorable. Probably the commonest form is that produced by an over-dose of digitalis. This can be recognized by the slow irregular pulse and the history of the treatment. The withdrawal of the digitalis leads to complete restoration of the rhythm and the patient promptly recovers without any subsequent impairment of the heart action.

A positive Wassermann indicates, of course, anti-syphilitic treatment which in some cases seems to relieve the condition. Two types of extra-systoles are recognized: auricular and ventricular. Ordinarily, they are brought about by a premature discharge of contractile energy, either of the auricle or the ventricle. In the former, the interval between two beats is greatly shortened and often afterward the interval is somewhat increased, but the ventricular complex shows the diaphasic stage and according as the characteristics are in the first and third leads of the right or left ventricular predominance, it can be assumed that the right or left ventricle harbors the pacemaker. In the absence of other forms of disease these patients are not in particular danger.

**Differential Diagnosis Between Mitral Stenosis and Aortic Insufficiency.** As an introduction to this subject, it is stated by E. H. Goodman,<sup>4</sup> that the fact that certain cases of mitral stenosis exhibit a diastolic murmur at the base, and certain cases of aortic insufficiency exhibit a presystolic murmur at the apex, makes the differential diagnosis between the two conditions a matter of some difficulty and of great interest.

In such a study as this two questions present themselves: First, what is the criterion, or what are the criteria which help one in the differential diagnosis? And second, how frequently does it become necessary to dis-

(4) Am. Jour. Med. Sci., April, 1919.

tinguish between mitral stenosis with a Graham-Steell murmur and aortic insufficiency with a Flint murmur.

In the study of men drafted into military service, such as was carried out by the present author, the history was of little value on account of misrepresentations by the recruit.

In a study of all patients in this work who had aortic insufficiency, rheumatism was encountered four times in the history, syphilis but once, and in six cases there was a history of neither.

Of the visual and palpatory findings in aortic insufficiency, it is pointed out first that the apex beat is displaced to the left, and may be as far as the fifth or sixth intercostal space downward. There is a tumultuous movement to the impulse which is not the quick circumscribed beat of a mitral stenosis. On palpation, the apex-beat humps itself under the hand, and the contraction is felt for some time, while in mitral stenosis the apex beat is suddenly felt as a single tap which recedes quickly and does not linger under the palm. No distinction can be made between the thrill of a stenosis and that of a Flint murmur, and if there is mitral insufficiency, as well as stenosis, the location and character of the apex beat are of little assistance in the differentiation of the two conditions. The cardiac outline is of much value. In all cases of aortic insufficiency, there is marked hypertrophy of the left ventricle, while in the pure stenosis, with no insufficiency, there is no hypertrophy, or but slight, if any. When mitral insufficiency is present, hypertrophy is generally seen, though not to the extent found in aortic insufficiency. The author has been impressed with the absence of hypertrophy as a valuable sign in differentiating between mitral stenosis and aortic insufficiency.

Under vascular signs, pulsating vessels are first considered. In aortic insufficiency there is marked pulsation of the carotid, radial, brachial and axillary arteries and these constitute a striking feature. In mitral stenosis this marked vascular pulsation is inconspicuous or absent.

In the second place, a pulse of a Corrigan type is not an uncommon feature of diseases other than aortic insufficiency. It has been found in mitral stenosis, but

never to the degree that it has been observed in aortic insufficiency.

Capillary pulse was observed in nine of the eleven patients who suffered from aortic insufficiency.

Traube's sign was present eight times. To obtain a systolic tone in the arteries, it has been found valuable to listen over the brachial artery at the bend of the elbow with the arm extended above the head. Euroziez's sign was present but twice, and was of little help in the diagnosis.

By a study of blood-pressure, there was found in the mitral-stenosis cases a difference between systolic pressure in the arm and the leg of from 40 to 50 mm. of mercury. In the aortic cases the difference may be as much as 130 mm. of mercury and in certain cases leg pressure is double that in the arm. When there is a difference of over 60 mm. of mercury, the lead is toward aortic insufficiency, although below 60 there is no certain proof that aortic insufficiency does not exist; also, high pulse-pressure in the arm and leg in aortic insufficiency is in marked contrast to the pulse-pressure in cases of mitral stenosis.

In discussing auscultatory signs, the author says that the character of the murmur is of little assistance as that of aortic insufficiency may closely resemble that of the **Graham-Steell**.

The apical murmurs of an aortic insufficiency and a mitral stenosis may resemble one another, but there is this difference that the Flint murmur is associated with a thumping, thudding first sound, whereas the true pre-systolic murmur of a mitral stenosis is followed by the **snappy first sound**.

In conclusion, Goodman points out that the most important features in favor of the diagnosis of aortic insufficiency are: First, the displacement of the apex beat, second, heaving feel of the apex impulse to the palpating hand; third, hypertrophy of the left ventricle; fourth, vascular signs, such as marked pulsation of the vessels, Corrigan pulse, capillary pulse, systolic tone in brachial artery with arm above the head, and fifth, blood-pressure increase of pulse-pressure, and marked discrepancy between the arm and leg pressures.



In favor of a mitral stenosis are the following:

Loud snappy first sound at the apex unless marked by an insufficiency of the mitral valves. Absence of apical displacement and of cardiac hypertrophy. Systolic tap or shock to the palpating hand. Absence of vascular signs. Absence of any characteristic blood-pressure phenomena.

**Left Scapular Pain and Tenderness in Heart Disease and Distress.** This article by J. Parkinson<sup>2</sup> is based on a study among soldiers, fifty of whom complained of pain at the lower end of the left scapula, associated with pain in the left submammary region. In picking out these fifty cases, eight of them were found among 100 consecutive instances of heart trouble among soldiers, but this number is not given as representing the true percentage: it is considered higher than the average. Patients who presented this symptom complained of pain in the heart, going through to the back, or pain at the heart and under the shoulder blade. The scapular pain was not found in the absence of submammary pain.

In describing the character of this pain it is said that it may be sharp and stabbing, or it may be dull and aching. Usually it partakes of the same characters as the accompanying submammary pain, although it is rarely so severe. Some patients talk of the pain going *through* to the back, and some of an aching pain going *around* to the back. Three complained of pain at the scapula before they mentioned that in front. Of the rest, one-third described it voluntarily, after the pain in front, and two-thirds mentioned it only when the question was put: "Any pain in the back; and where?" The location of the pain was indicated by the patient himself, as is clearly indicated in the accompanying illustration (Fig. 12).

Exertion was found to be by far the greatest exciting cause. The pain in front and at the back was said to be worse on exertion, or present on account of exertion, in forty-five of the fifty patients.

The duration of the submammary pain had been longer than five years in twenty-five instances, between

one and five years in eighteen, and below one year in eight only.

The most constant symptom associated with the thoracic pain was shortness of breath, also dependent on exertion, and it was present in all but two cases.

It is well known that the pain of heart affections may be accompanied by hyperalgesia of the chest, but it is often forgotten that this hyperalgesia is to be found on the posterior surface as well as on the anterior.

Ten of these patients showed hyperalgesia on the posterior surface of the chest, the extent of which is indicated in the following tabulation.

Anterior	Posterior
1. II. space to I. costal margin.	1. Spine of scapula to IV. space.
2. I. space to umbilical plane.	2. Spine of scapula to loin.
3. Nil.	3. Lower angle of scapula (to finger pressure only).
4. IV. and V. spaces.	4. Lower angle of scapula (finger pressure only).
5. I. space to umb. plane.	5. Spine of scapula to loin.
6. III. to V. spaces.	6. Region of angle of scapula.
7. II. to VI. spaces.	7. Spine of scapula to IX. space.
8. IV. space to below umb. plane.	8. Spine of scapula to loin.
9. V. space.	9. Lower angle of scapula.
10. III. to VI. spaces.	10. Lower half of scapula.

Whatever is capable of producing chronic pain below the left breast appears to be also capable of producing pain at or about the lower angle of the left scapula. It is therefore seen in valvular disease of the heart, myocardial disease and in arteriosclerosis and chronic nephritis, when the heart has become burdened.

Among these patients, a history of rheumatic fever was obtained in twenty out of the fifty. Of these, ten proved to have signs of valvular disease. Only two men gave a history of syphilis.

From these observations it is learned that pain at the lower angle of the left scapula often supervenes in the course of chronic pain below the left breast, especially when this is severe and of long standing.

The causes of left submammary pain, as also of left scapular pain, include valvular and myocardial disease.

arterial and renal disease, especially with high blood-pressure, functional heart disorders, with or without nervous symptoms, and general ill-health where the symptoms suggest cardiac distress. It is therefore present in many cases of "soldier's heart."

The sixth thoracic spinal segment, alone or in combination with the fifth, supplies the submammary and infrascapular regions where pain is commonly felt in these



Fig. 12. Typical posture in complaint of left scapular pain.

heart affections. The accompanying hyperalgesia may be limited to the distribution of the sixth or fifth and sixth segments, but it often extends to a larger area and occasionally even to that representing most of the segments of the thoracic cord.

This submammary pain and hyperalgesia of chronic heart affections with extensions to the left scapula forms a contrast in many respects with the sternal and supra-mammary paroxysmal pain of angina pectoris with extensions to the left arm.

If hyperalgesia persists or recurs frequently in the

course of chronic heart disease or disorder, it indicates a new and troublesome phase. Hypersensitive tissues are not merely concomitant, they induce and supplement pain. It is now provoked even by slight pressure or tension, such as by lying on the left side or turning over in bed, or by taking a deep breath, which otherwise would not produce characteristic cardiac pain.

**Disordered Action of the Heart.** A paper by J. A. Venning,<sup>6</sup> dealing with the etiology of disordered action of the heart, is based upon a report on 7,803 patients. The object is to analyze and draw some conclusion from the study of these patients who were admitted to an army hospital suffering from a condition diagnosed as "disordered action of the heart, D. A. H.," or "valvular disease of the heart, V. D. H."

The difficulty of obtaining an accurate analysis of the patient is emphasized. The author had to be guided largely by the man's history as given by himself. In some instances it was impossible to know to which of several factors the symptoms should be ascribed. For instance, a man after a considerable time in the front lines might get a dose of gas which incapacitated him for a day or two only, and might afterward develop persistent symptoms of D. A. H.

The question arises: Are those symptoms due to strain, physical and mental, the gas being merely the last straw affecting possibly his mental state rather than his physical condition, or is the gas solely to be blamed? Venning takes the view in such cases that gas is merely the last incident, and is not the real factor. Just as in the case of a man being blown up by a shell bursting near and symptoms of neurosis following, the being blown up is merely the last straw. It is the previous mental struggle and strain which are the real causes.

Infections come easily second as a cause varying in each period of six months very slightly, namely, from 20.3 per cent. to 22.4 per cent., and by far the greater number of these were due to infections in civil life and not to P. U. O., or pyrexia of unknown origin, as has been widely held.

---

(6) Brit. Med. Jour., Sept. 13, 1919.

The most crippling infection, and that producing permanent disability of varying degrees, is found to be rheumatic fever. It accounted for from 40.7 up to 56.7 per cent. of the total cases of infection.

It has been asserted that trench fever accounts for over 50 per cent. of all D. A. H. cases. This was found by Venning to be far from the case. Infections account for about 21 per cent. of all cases, and of the infections, pyrexia of unknown origin accounts for from 6.4 per cent., in the first six months of this study, up to 23.2 per cent. in the last period, which was at the end of two years from the first period. The conclusion reached from this analysis is that the strain, mental and physical, of warfare is the chief cause of the symptoms of disordered action of the heart: and that the causation of next importance is infectious diseases, and of these, the majority were due to those contracted in civil life, rheumatic fever being the worst offender.

There are extensive figures and tabulations presented with this article, which can not be included here.

**Effects of Epinephrine Injections in Soldiers with Irritable Heart.** The study that is reported here by J. T. Wearn and C. C. Sturgis<sup>7</sup> was made to determine the relation of the thyroid gland to conditions described by DeCosta during the Civil War as irritable heart of soldiers, and termed by Lewis, during the recent war, as effort syndrome.

First, a study of the basal metabolism in a number of soldiers who presented this condition was made at the United States Army General Hospital Number 9. From this study it was concluded that hyperthyroidism did not play a significant rôle in the production of the symptom-complex of irritable heart of soldiers.

In order to make the investigation of the rôle taken by the thyroid gland more comprehensive, it was decided to employ at the same time the epinephrine test.

This was carried out by placing patients at absolute rest in bed for a period of one hour, or longer, if necessary, in order to have them quiet, and have blood-pressure and pulse at or near a normal and constant rate. After this period of rest, control readings of blood-pres-

(7) Archiv. Int. Med., September, 1919.



sure, pulse and respiratory rate were made at five minute intervals. Also, at this time note was taken as to the presence of nervousness, precordial pains, dizziness, palpitation or any other symptoms which are significant, and which might be considered significant. Likewise, the objective condition of the patient was observed and was recorded if any of the following signs were present: Tremor of the hand, sweating, coldness of the hand, throbbing of the neck, epigastrium or over the precordium, and pallor or flushing.

After satisfactory control readings were made, 0.5 c. c. of a 1:1,000 solution of epinephrine freshly prepared, was injected into the deltoid muscle. After the injection, four or five readings were made of blood-pressure, pulse and respiratory rates, at two or three minute intervals, and also at these times any change in the objective or subjective condition of the patient was noted. After the first two observations readings were continued at five minute intervals, until one hour after the injection, when ten minute readings were made for a period of one-half hour, thus making the observation period one and one-half hours from the time of the injection.

In describing the reaction to epinephrine, the authors state that a typical positive reaction manifests itself on an average in about twelve minutes after the injection by a rise in systolic blood-pressure, increased pulse-rate, and certain characteristic changes in the subjective and objective conditions of the patients. There may be restlessness, complaint of nervousness, precordial pains, palpitation and frequently apprehension. Pallor or flushing may be present. A fine tremor is very characteristic and while it usually only involves the hand, it may become general and very marked, occasionally to the extent of shaking the bed. In a number of instances in this work there was tremor of the eyelids. The hands usually became cold, and often there was excessive sweating, especially in the palms. Other changes noted irregularly were dilatation of the pupils, pulsation in the neck and epigastrium and over the precordium, and frequently the patient would state that he experienced about the same symptoms that he had previously noted after exertion. The conditions just mentioned are con-

sidered by the authors very characteristic, and when they are present a hypersensitiveness to epinephrine is easily recognized without the aid of the blood-pressure or pulse record.

In this work seventy-three patients with symptoms of irritable heart were studied. Their symptoms were of long duration and for the most part, antedated their entrance into military life. Of this group about 60 per cent. gave a reaction which definitely indicated a hypersensitiveness to epinephrine. It is known that epinephrine has a selective action on the sympathetic autonomic nervous system. It may be suggested, therefore, that the symptoms and signs induced in the positive cases are the result of a hypersensitive sympathetic autonomic nervous system. A careful clinical analysis of the patients showing positive and negative reaction, however, revealed no essential clinical differences between the two groups. One can not state that the clinical condition of the patients who are sensitive to epinephrine depends in any way directly on the factors underlying the positive reaction. On the other hand, this is not at all impossible, as there is nothing to lead one to conclude that the factors causing the symptoms in the positive and negative groups are the same.

Patients of this class are not true products of war, for they are seen in civilian as well as in military life. They are of a type that go from one out-patient clinic to another with complaints of nervousness, weakness, palpitation, precordial pain and dyspnea. They are classed as neurotics or neurasthenic individuals, and have usually been receiving medical attention for years. As a class they have assumed a new importance since their induction into the army. There seems to be a certain level of strain below which these people can live without symptoms, and their one effort in life is to keep below this level. Above it their symptoms appear and they break. This explains why they are found in the army as a class and not in civil life as such. In both places, however, they present a problem of no little importance to the internist and to the practitioner of general medicine.

**Effects of Epinephrine on Basal Metabolism in Soldiers with Irritable Heart.** In the investigation at General Hospital No. 9 on patients showing the symptom-complex of the irritable heart of soldiers, it was found that a considerable percentage of them were also hypersensitive to epinephrine. Careful clinical analysis, however, as well as determinations of the basal metabolism did not lend any support to the theory that hyperthyroidism was an underlying feature in the condition. It was hoped, therefore, that a study of the basal metabolism under the effects of epinephrine would assist in the explanation not only of why there was a response to the drug in any of the cases of irritable heart, but further as to why this response was evoked in only a certain percentage of the patients. This work was carried out by E. H. Tompkins, C. C. Sturgis and J. T. Wearn.<sup>8</sup> They considered it necessary to study not only the cases of irritable heart, but also a group of normal individuals for comparison.

For this purpose, men with simple organic heart lesions, as well as admittedly normal men seemed a most satisfactory contrast to the "irritable heart" group. Those with hyperthyroidism on the other hand present the best pathologic contrast.

The epinephrine tests were carried out essentially along the line stipulated by Goetsch and described in the preceding abstract.

Four groups of subjects were studied. Two of these groups were epinephrine negative and two of them were epinephrine positive.

The first group consisted of normal subjects and of patients with "effort syndrome" who did not react to epinephrine.

The second or positive group consisted of patients with effort syndrome who reacted to epinephrine and a small series of patients who had hyperthyroidism.

It was found with unbroken regularity that metabolism showed a rise after the injection of epinephrine. This was true in the normal as well as in the pathologic cases. It was true whether there was any other sign of reaction or not. This increase in metabolism, however, was far

(8) Archiv. Int. Med., September, 1919.

more marked in those patients with a positive than in those with a negative reaction. With but one exception, every positive reaction was accompanied by a rise in the metabolism of 20 per cent. or over. On the other hand, no negative reaction showed a rise above 20 per cent. and, on the whole, not above 15 per cent. The increase in metabolism is expressed by a greater oxygen deficit in the expired air, but far more by an increased amount of air breathed as shown by the greatly augmented minute volumes. This increase in the minute volume was as invariable as was the rise in metabolism. The amount of air breathed a minute was increased as much as two liters in a considerable number of cases.

In the positive cases, one metabolism period was taken as nearly as possible at the height of the epinephrine reaction and it was at this point that the greatest metabolic increase was found. The negative cases, while never giving a metabolic response equal to that at the apical point of the positive cases, showed a tendency to reach their maximum of change at a period earlier than at the time of apical change in the positive cases. The authors say that any interpretation to be based on changes in the respiratory quotient must always be made with due consideration of the mechanical factors that may influence the quotient in periods as short as those in the method used in this work. With these factors in mind, they are inclined in this report to disregard the respiratory quotient as of any value in showing changes in the percent usage of the food stuffs.

Of the various possible explanations of this increase in metabolism the most probable cause in the opinion of the authors is the hyperglycemia due to the action of epinephrine. Carbohydrate plethora results in increased metabolism, which is at the expense of the carbohydrate as shown by the simultaneous elevation of the respiratory quotient. The elevation in the metabolism and the respiratory quotient under epinephrine can thus very positively be attributed to the known hyperglycemia resulting from the epinephrine.

The possibility of epinephrine as a direct stimulant to cellular metabolism in general is said to have but little evidence for or against it. It is generally accepted, how-

ever, that epinephrine has a definitely selective action on the sympathetic autonomic nervous system, and it is probable, therefore, that epinephrine acts indirectly in causing an increase in the metabolism and it is by acting through the sympathetic system that it produces the changes—the tremor, hyperglycemia, etc.—which are probably the actual causes of the increased heat output.

**Effect of Epinephrine on Electrocardiogram of Patients with Irritable Heart.** The effect of epinephrine on the circulation has led to an investigation to determine whether or not electrocardiographic tracings show any changes during the occurrence of the circulatory changes.

Eighteen patients with irritable heart were studied in this work, which was carried out by H. D. Clough,<sup>9</sup> in conjunction with J. T. Wearn and E. H. Tompkins, who were making metabolism studies on similar patients.

The results obtained are summarized as follows:

The effect of epinephrine has been observed in normal individuals and in a number of patients with the symptoms of "irritable heart." All the latter were hypersensitive to epinephrine in the sense that they gave a much more pronounced reaction to a small dose of the drug than did normal individuals.

In some cases, gross abnormalities of the electrocardiographic record were observed. The following were the most important deviations from the normal: Changes in conduction (delayed conduction, partial heart-block) and the production of ventricular extrasystoles.

Special studies were made of the effect of epinephrine on the conduction time, length of systole and height of the *T*-wave in twelve epinephrine hypersensitive patients with "irritable heart" and in twelve normal men. No changes were found in the conduction time or the length of systole in either type. In both at the height of the reaction there was a decrease in the height of the *T*-wave.

An attempt has been made to correlate the symptoms complained of by the patients with "irritable heart" at the height of the reaction with abnormalities of the electrocardiogram, but no definite association could be made.

(9) Archiv. Int. Med., September, 1919.



**Rare Types of Bradycardia.** Details of three cases are furnished by Mougeot:<sup>10</sup>

1. Apparently complete auriculo-ventricular dissociation, dissipated either by atropine or epinephrine.

2. Total sinusual bradycardia—a rare form—refractory to the tests by atropine, amyl nitrite, and ocular compression.

3. The nodal bradycardia (of Mackenzie), for which this latter author suggests the presence of a total sino-auricular block.

**The Cardiovascular Defective.** In a study of the cardiovascular defective, Louis M. Warfield,<sup>1</sup> Professor of Clinical Medicine, Marquette University Medical School, Milwaukee, states that before the late war the number of such cases apparently was not great, and the lack of any somatic lesions caused physicians to regulate them into the motley group composing neurasthenia. "For most of us to call a group of symptoms neurasthenia was an admission of diagnostic limitations. We felt that because so many persons loosely termed neurasthenies were found on careful study to have definite pathologic lesions which could account for their nervous instability, all cases of neurasthenia should show some pathologic basis. We very probably erred in swinging the pendulum too far on the physical side and neglecting too much the purely mental reaction of the patient."

The great variability of persons in their emotional spheres and in their subconscious reactions to varieties of stimuli certainly have not been appreciated by most physicians. The inhibitory effects of training at home and in school were little considered. Inheritance, although stressed by too many recent writers, did not have the place that it deserves in the summation of the factors which make a diagnosis. It was not that all these terms were not known and comprehended, it was that their full significance was neither fully understood nor fully appreciated.

Certain characteristic symptoms are found in all the cardiovascular defectives. These are symptoms from which many men suffer when put through violent exer-

(10) Presse méd., Feb. 4, 1920.

(1) Amer. Jour. Med. Sci., August, 1919.

tion. The differentiation between the defectives and the normal men is largely one of degree. Exercise of the lightest character serves to bring out in the defectives an exaggeration of all the symptoms of exhaustion. Typically, after slight exertion the men become breathless, giddy, have pain over the precordium, palpitation of the heart, and a feeling of utter exhaustion. Frequently they have headache, are sleepless, rest at night really does not rest them, and they have clammy, cyanosed hands and feet. They sweat profusely in the axillae and have a mottled skin and unstable vasomotor reaction.

The author states that at Jefferson Barracks, Missouri, where the study was made on which this article is based, no attempt was made to cull out these defectives before they were taken into service.

Three hundred and fifteen cases were carefully studied and 158 exercised in the hospital. In 297 cases the records were complete enough for later use.

The disposition of the cases at examining barracks is given as follows:

#### DISPOSITION OF CASES AT EXAMINING BARRACKS

- 60 cases (37.0 per cent.) diagnosed hyperthyroidism, rejected.
- 47 cases (29.0 per cent.) diagnosed pulmonary tuberculosis, rejected.
- 52 cases (32.0 per cent.) diagnosed irritable heart, rejected.
- 2 cases (1.2 per cent.) diagnosed cirrhosis of the liver, rejected.
- 1 case (0.8 per cent.) diagnosed bronchial asthma, rejected.

#### DISPOSITION OF CASES OBSERVED IN HOSPITAL

- 40 cases (29.6 per cent.) no lesion found, normal, accepted.
- 17 cases (12.6 per cent.) diagnosed hyperthyroidism, rejected.
- 47 cases (34.8 per cent.) diagnosed pulmonary tuberculosis, rejected.
- 29 cases (21.5 per cent.) diagnosed irritable heart, rejected.
- 2 cases (1.5 per cent.) diagnosed cirrhosis of the liver, rejected.

It will be seen that cases of pulmonary tuberculosis and hyperthyroidism (including exophthalmic goiter) composed the greater proportion of the two groups. As a matter of fact the symptoms complained of by men are so similar in the cases of the diseases named above and irritable heart that it is only after the most careful study that the cases can be separated into the proper group.

These cases of irritable heart, the cardiovascular defectives, fall into three groups:

*A.* Strictly cardiovascular:

1. Following infectious disease. Chronic myocardial degeneration.
2. Existing since childhood. (*a*) Associated with poor mentality; (*b*) associated with good mentality.

*B.* Some defect in endocrine secretion:

1. Hyperthyroidism.
2. Exophthalmic goiter.

*C.* Associated with definite somatic lesions:

1. Pulmonary tuberculosis.
2. Hodgkin's disease.
3. Focal infections: chronic.
4. Other diseases: cirrhosis of the liver (hook-worm), asthma, etc.

In a summary the author states that there is a class of young men of usually healthy appearance who, nevertheless, suffer from a group of symptoms following mild exercise characterized by breathlessness, precordial pain, dizziness, palpitation, and exhaustion. There also may be headache, sleeplessness, cold, clammy hands and feet and profuse sweating. These men might never have been discovered except for the army draft, which caused thousands of young men to be examined physically. These men have no complaints, as a rule, which lead them to seek medical advice. They find that they are better able to make a living at light or secondary work than at hard work, so they drift into the lighter occupations. The majority are surprised when told that there is something the matter with them, although they have recognized the fact that they can not take the violent exercise which other men of their acquaintance can take. A certain number are taken by their parents to a physician, who may diagnose heart disease or neurasthenia.

There is no common etiologic factor among the true cardiovascular defectives—no cause can be found except a constitutional inferiority, a poor quality of tissue, which must be supposed to account for the syndrome.

Among others, certain chronic diseases or the result of severe, acute illnesses are responsible for the syndrome.

When there is a definite pathologic basis, such as pulmonary tuberculosis or chronic focal infection, etc., cure of the disease causes the effort syndrome to disappear. Cases resulting from infectious disease or based upon constitutional inferiority, do not improve, according to the author's experience.

Exercise was valuable in determining the fitness of the men for military duty and in giving data in the diagnosis of certain cases suspected of being tuberculosis. The cases were studied primarily for the purpose of sorting the fit from the unfit in military service. Happily, this need no longer be done. However, the knowledge gained in observing these cases is not devoid of value to civilian life. It should materially assist in handling a group of cases hitherto poorly classified and insufficiently studied.

**Auricular Flutter and Its Treatment.** The definition of auricular flutter as given by J. Meakins,<sup>2</sup> of Montreal, is that it is a specific form of auricular tachycardia in which the auricular rate is over 200 a minute, and frequently in the region of 300 a minute. Associated with this, there is a partial heart-block; consequently the ventricular rate may be one-half, a third, or even less than a fifth the rate of the auricle. The pulse is not necessarily regular; in fact it is frequently irregular, which is due to the ventricle responding to an irregular ratio of the auricular contractions. It is quite distinct from auricular fibrillation, although there is a close relationship between them. Its distinction from auricular tachycardia of a slower rhythm is more or less arbitrary, but it is essential, until more is known concerning the pathology of all forms of auricular acceleration.

Auricular flutter is much commoner than is usually thought. The reason being that thorough systematic examinations are not made in all cases of constant or intermittent tachycardia. The more diligently this condition is looked for, the oftener it is found.

It may be recognized in a variety of ways. The most conclusive method of recognition is by the electrocardio-

---

(2) Canadian Med. Ass'n Jour., July, 1919.

graph. Here there is usually found a complex of distinctive characteristics. The outstanding feature in the symptomatology of this condition is tachycardia. This may be present week in and week out for long periods. As a rule, however, it is intermittent, occurring after exertion of more than a limited amount. Auricular flutter usually occurs in patients over the fortieth year, although a few cases have been reported under this age.

The treatment consists in the use of digitalis in large doses until auricular fibrillation occurs, and then if the digitalis be stopped, the tendency is for the normal rhythm to return. Failure of cure is usually due to one of three causes: first, intolerance of digitalis by the patient; second, cessation of treatment at too early a date; and third, inability to produce fibrillation before toxic symptoms appear even when the digitalis is tolerated in large doses.

If once the abnormal rhythm of flutter has been displaced by normal rhythm, it is rare that the pathologic condition returns. If it does, it will be within a few days of the re-establishment of the normal rhythm. Another course of treatment will promptly repeat the cure. More than one recrudescence of flutter is extremely rare.

There are a certain number of cases in which a cure is not possible. Among these are the individuals who have an intolerance to digitalis, toxic symptoms being produced by comparatively small doses. There are other patients in whom digitalis may be given in very large doses before toxic symptoms appear, without auricular fibrillation being produced. In such cases a complete cure is not possible. But relief may be obtained by taking small doses of digitalis constantly, as in auricular fibrillation. The digitalis reduces the conductivity of the auriculo-ventricular node, so that a 4-1 or 5-1 heart-block may be almost constant in spite of accomplishing considerable physical exertion. Under such circumstances these patients enjoy a comparatively comfortable and useful life.

The records of patients in the author's practice are presented to verify the points brought out in this article.

**Digitalis in Treatment of Auricular Fibrillation.** The rapidity and the persistence of the action of digi-



talis on hearts showing auricular fibrillation is discussed by G. C. Robinson.<sup>3</sup>

In this work the dose amounting to 15 c. c. of the tincture of digitalis per hundred pounds of patient was the maximum, and was usually given as a single dose, although in some of the earlier cases the dose was divided into three or more parts given from four to six hours apart. The clinical results obtained in giving large single doses of the drug to about 100 patients have been convincing of the correctness of Eggleston's work. The doses usually ranged from 15 to 25 c. c. of the tincture.

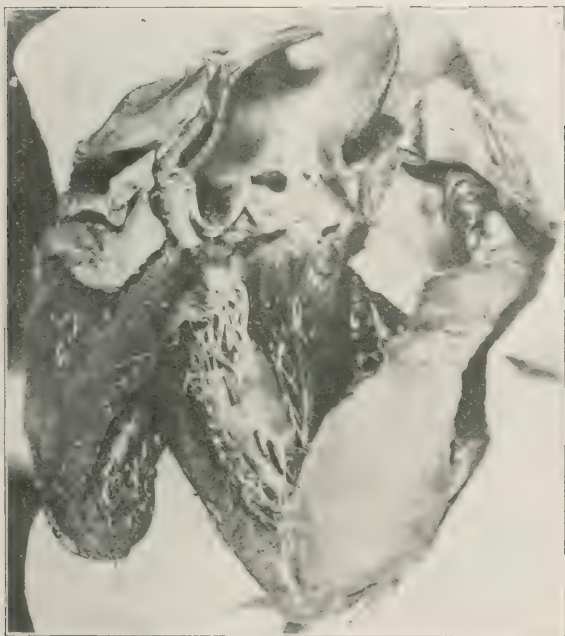
The patients were studied during continuous rest in bed. The heart rate was counted several times a day by a member of the medical staff of Washington University School of Medicine, St. Louis, using the stethoscope over the heart. This was done for a number of days whenever the withholding of the drug seemed justified. The radial pulse was also counted and these findings together with the pulse deficit, the difference between the heart and radial rates, were charted. After the digitalis was given, similar counts were frequently made, in some cases at 15-minute intervals for several hours.

The well-known effect of digitalis in slowing the ventricular rate in cases of auricular fibrillation was used as indicating the action of the drug, and practically all the cases reported in this paper showed an abnormally high ventricular rate before digitalis was given. Two cases of auricular flutter are exceptions to the foregoing procedure, and here the disappearance of flutter as demonstrated by electrocardiograms was taken as evidence of digitalis action. Twenty-six cases were studied and tabulated. To these twenty-six patients, suffering from auricular fibrillation or flutter, large single doses of the tincture of digitalis were administered by mouth. The drug used was standardized and was given usually in doses ranging from 15 to 25 c. c.

A study of these cases demonstrates that such doses of digitalis affect the heart in cases of auricular fibrillation or flutter at a relatively constant time after administration, in from two to five hours, indicating that the

(3) Proc. Ass'n Amer. Physicians, 1919.

PLATE XIII.



Photograph of the heart, showing aortic valve with extensive lesion on one cusp. On the inner surface of the cusp is seen a vegetation, while at the base of the outer surface there is a small, deep ulceration. Smears from this showed many meningococci. Stone and Brown, page 341.



drug is absorbed from the alimentary tract at a fairly rapid and uniform rate.

This series of cases also demonstrates that the maximum effect on the heart is usually obtained at about twenty-four hours, and generally continues to be effectual for from four to fifteen days, or an average of nearly ten days.

**Action of Digitalis on the Rheumatic Heart.** There is still considerable difference of opinion as to the exact action of digitalis on the heart, and the exact type of case in which it is suitable. In auricular fibrillation, all are agreed that digitalis acts beneficially, and this is no new discovery, for it was in the type of case known as auricular fibrillation that digitalis established its reputation many years ago.

A point at issue between Sir John Broadbent and Dr. Thomas Lewis is as to whether digitalis ever acts beneficially on a regular heart, that is, a heart in which normal rhythm is present. The question of rapidity of action is not referred to.

The purpose of the present paper by G. A. Sutherland,<sup>4</sup> is to show that a regular heart showing signs of a failure may be beneficially acted upon by digitalis. In the experience of the author, such an effect is produced only when the heart is acting rapidly, and the mode of action consists solely in slowing the cardiac rate, thus leaving the ventricles free to contract more powerfully.

In regard to the action of digitalis on the heart with a normal rhythm, Sir James Mackenzie drew the following conclusions:

“So far as slowing of the heart’s rate is concerned, it may be laid down as a law, that the reaction to digitalis is far less effective when the rhythm is normal than when there is auricular fibrillation.

“While there is no doubt that digitalis relieves distress of breathing and reduces dropsy, it does not do so necessarily by slowing the pulse. The rate of the heart in cases of aortic regurgitation with the normal rhythm, is not affected, or very slightly. . . . In patients with the normal rhythm digitalis has induced irregularities of the heart’s action of the following forms: (1) sinus ir-

(4) Quart. Jour. Med., April, 1919.

regularities, (2) extrasystoles, (3) partial heart-block, (4) pulsus alterans.

"In cases with the normal rhythm the improvement was not very marked as a rule, and in most of them it is doubtful whether the rest alone was not sufficient to account for the slight improvement."

Mackenzie has also shown the effect on the heart rate in a series of cases of auricular fibrillation, and in another series of cases of normal rhythm, both of which were treated with full doses of digitalis. In the former, the average heart rate at the beginning of the treatment was 112, and at the end it had fallen to 64. In the latter, the initial heart rate was 78, and at the end of the treatment it was 75. In the former class the average heart rate per minute was lowered by forty-eight beats, and in the latter by three beats. He would seem to have established the fact that a heart beating with a normal rhythm at a normal rate firstly, is not affected to any appreciable extent, as regards the rate by medicinal doses of digitalis, and secondly is not beneficially acted upon by digitalis. These conclusions have been confirmed by Sutherland's own experience. He desires in the present paper to show that there is a class of cases with the persistently rapid and regular heart rate, due to rheumatic infections, in which the acceleration can be controlled by digitalis in medicinal doses. Further, he asserts that this action is as specific as in the treatment of auricular fibrillation and the beneficial effects are as striking.

The type of case selected is next described. Among those who have passed through an attack of acute or subacute rheumatic infection, there are many individuals who show a persistently accelerated cardiac rate, up to from 115 to 130 beats a minute. It must be assumed that if the cardiac acceleration is not nervous in origin, there is probably some myocardial change, organic or toxic, disturbing the normal pacemaker.

If active signs of rheumatic infection were present, as indicated by a temperature above 99° F. to 100° F., digitalis was not given in any of these cases until the temperature had been reduced by means of salicylate of soda or had fallen to normal.



The patients were all under the age of 14 years. In all the cases rheumatic infection had undoubtedly been present, and, so far as could be determined, there was no mixed infection at the time. A nervous source of disturbance was ruled out by the fact that the heart rate was as rapid during sleep as during waking hours.

In cases of this class the question may arise: why is treatment by digitalis called for? It may be urged that under rest in bed accelerated heart rate will in time settle down. Rest in bed has its disadvantages, however. indefinite prolongation of rest in bed is by no means suited to the healthy growth and development of a child.

Considering the mode of action of digitalis in slowing the heart rate, Sutherland states that in the cases dealt with in this work there is one constant factor, namely, rheumatic infection, and experience has shown that it is on the rheumatic heart that digitalis has its most potent action. The conclusion reached as to the mechanism of the increased heart-rate was that acceleration was due to the activity of the sino-auricular node having been directly affected by the rheumatic infection. When the auricular and ventricular rates are similarly increased, and the arterial and venous tracings show a regular and normal rhythm, as they did in these cases, it may reasonably be assumed that the acceleration of rate is due to some disturbance of the normal action of the sino-auricular node. The only direct method of slowing the heart-rate, as a whole, seems therefore, to be by an inhibitory action on the sino-auricular node.

The assumption that digitalis acts on the heart through stimulation of the inhibitory action of the vagus serves very well as a basis for clinical work. It was recognized that in order to check the over-action of the sino-auricular node full doses of digitalis would probably be required, as former tests with small doses continued over a long period had failed to give any results.

There follows a long discussion of clinical methods and results. The conclusion reached from the study is to the effect that the author has proved to his own satisfaction that in the type of case described, one can prescribe digitalis with as much confidence in its efficient and beneficial action as in cases of auricular fibril-

lation. In the former digitalis is given with a view to its acting on the sino-auricular node, while in the latter its action is directed to the auriculo-ventricular node and bundle. In both cases the object aimed at and attained by means of digitalis is a slowing of the ventricular rate, and provided that there is a sufficiency of sound contractile tissue in the ventricles, the natural powers of the heart are then capable of restoring a weakened or failing circulation.

#### **Digitalis in Cardiac Cases with Regular Pulse-Rate.**

That satisfactory effects in cardiac cases with regular pulse-rates can be obtained by digitalis therapy is shown by H. A. Christian.<sup>5</sup> He states that cardiac patients with broken compensation usually improve with rest, but hospital rest alone does not give the result obtained later when it is combined with digitalis therapy. The chief factor in the failure to get good results from digitalis lies, Christian thinks, with the improper use of that drug; most commonly the dosage given is insufficient.

Concerning the danger of giving too much digitalis, the author states that in an extensive hospital experience with cardiac diseases he can not recall a single instance admitted from the care of an outside physician in which too much digitalis had been given. On the contrary, he has seen a number of patients sent to the hospital merely because they were doing poorly, on account of the fact that the attending physician was giving too little digitalis. The insufficient dosage of digitalis frequently is due to the fact that the digitalis preparation is far below the standard pharmacopeial strength. In the usage of digitalis, the preparation played no part. The author has long since learned that the powdered leaf made freshly into pills is as satisfactory a form of digitalis as either tincture or infusion; and, if the leaf is good, just as effective as digipuratum and digifolin and far less expensive.

Another cause of too small dosage of digitalis lies in the common practice of prescribing tincture of the drug by drop, and counting a drop as a minim; whereas, it generally takes two or three, or even more, drops to make a minim. Digitalis should be prescribed in weight or in

(5) Amer. Jour. Med. Sci., May, 1919.

measured amounts, not by drops, and enough should be given of a reliable preparation to produce a definite effect at least within four days; usually an effect is noted in half this time.

In his experience with chronic myocarditis, Christian has obtained most excellent results from adequate digitalis therapeutics, and there are no contraindications to its use, for even in those cases advanced beyond the bound of a therapeutic response no bad effects followed digitalis.

He pointed out that the most brilliant results of digitalis therapy are seen most commonly in individuals with auricular fibrillation; but he has seen frequently just as good results in chronic cardiac cases with edema, in which there was no irregularity of the pulse, or only an occasional extrasystole.

**Meningococcus Endocarditis.** This report is based on a single instance of meningococcus endocarditis observed by M. C. Stone and W. D. Brown.<sup>6</sup>

The patient, a man, 24 years old, was admitted to a military hospital, where a diagnosis of meningococcus meningitis was made, this diagnosis being based on the spinal fluid findings, and physical examination of the patient.

Intraspinous and intravenous serum treatment were administered and the patient apparently recovered. Twelve days after he was admitted to the hospital, a purpuric spot about the size of a dime was observed on the dorsum of the right hand, and another on the outer surface of the left ankle.

The man developed severe headaches and numerous additional purpuric spots appeared on the hands and feet.

The treatment was resumed, and after three days, there was a marked degree of improvement. A second relapse occurred four days after the first one, and this relapse was preceded by a purpuric rash also. He continued to have similar relapses, each one being preceded by a rash, until he died one month after he was admitted to the hospital.

At autopsy there was found over the base of the brain about the circle of Willis, and over the surface of the pons, a moderate amount of yellowish exudate beneath the pia, which itself was thickened and adherent. The fluid escaping from the spinal canal was moderately in excess, but not especially cloudy. There were numerous minute hemorrhages over the surface of the cerebellum near the pons. The dura covering the base of the skull was notably injected, but showed no exudate.

The spinal cord and membranes presented practically no gross changes.

There was slight enlargement of the heart, apparently due to hypertrophy of the left ventricle. All the cavities contained fibrin clots. The valves were normal, with the exception of the aortic. The posterior cusp was the site of a pinkish irregular vegetation, flesh-like in consistency, and with a broad base measuring 1 cm. in diameter. The edge of the cusp was free, the lesion occupying the base and involving both surfaces. The outer portion of the lesion was ulcerated into the heart wall for a distance of several millimeters. Other minute vegetations were seen on this and the adjacent cusps. There were a few atheromatous areas on the ascending aorta.

Smears from the ulcerated base of vegetation on the heart valve showed many Gram-negative diplococci.

The anatomic diagnosis included leptomeningitis and pachymeningitis (subacute) of the brain and spinal cord; incipient pericarditis and acute endocarditis; petechiae of the skin, the stomach, the omentum and the pelvis of the kidneys.

The cause of death was said to be cerebrospinal fever.

The condition found in the heart is shown in Plate XIII.

**Endocarditis Due to Bacillus of Influenza.** During the twelve months ending December, 1917, there occurred in a base hospital in France, nine fatal cases of bronchopneumonia in which the influenza bacillus was recovered from the lungs at autopsy. In all of these, save the first two, a clinical diagnosis of influenzal bronchopneumonia was made before death. Three of these cases presented complicating lesions of the circulatory system; one a purulent pericarditis, and two an acute endocarditis due

to the influenza bacillus. It is the purpose of the present paper by A. Malloch and L. J. Rhea,<sup>7</sup> to place on record a description of the two latter cases.

The first patient was a man, aged 39, admitted on the third day of the disease with a diagnosis of bronchitis. Dyspnea and pain on the right side of chest were prominent. Other items included in the summary of the case are signs of a consolidation of the right lung and of the left base. On the sixth day, a diagnosis of lobar pneumonia was made, but it was changed on the twelfth day to confluent influenzal bronchopneumonia because of the finding of *B. influenzae*, as the predominating organism in the sputum. Examination of the heart was negative, the temperature was subnormal. Respiration and pulse were very rapid. There was heavy sweat. Death occurred on the thirteenth day.

Postmortem examination was as follows: Bilateral confluent bronchial pneumonia; dilated right heart; syphilitic aortitis, also involving the aortic ring; acute vegetative endocarditis of aortic cusps; mild chronic interstitial nephritis. *B. influenzae* was grown in pure culture from terminal bronchioles from heart's blood and from vegetations on aortic cusps.

A summary of a second case is as follows:

A man, aged 44, was admitted on the fourth day of the disease, with a diagnosis of bronchopneumonia, which came on with a chill after getting wet. There were cough, pain in the chest, dyspnea, cyanosis, and signs of capillary bronchitis. The case was diagnosed as influenzal bronchopneumonia on account of the nummular character of the sputum and the presence of *B. influenzae* as the predominating organism in it. The heart was enlarged, and there were no murmurs. Dyspnea and cyanosis increased. Sweats and septic temperature followed and the patient died on the sixth day. At postmortem examination there were found: Bilateral capillary bronchitis and bronchopneumonia; dilatation of the right heart, with hypertrophy of both sides; old endocarditis of the aortic cusps; acute vegetative endocarditis of the aortic cusps and otherwise healthy mitral cusps; large septic spleen; slight chronic interstitial nephritis. Cultures from the

(7) Quart. Jour. Med., April, 1919.



terminal bronchi and from the center of the aortic vegetation yielded *B. influenzae* in pure culture. The cultures from the heart's blood were negative.

From the literature, the authors have collected records of forty-five cases of endocarditis occurring in connection with influenza infection in which there was more or less evidence pointing to the influenza bacillus as the cause of the lesion. In only fourteen of these cases were the data sufficiently conclusive to justify an absolute diagnosis of influenzal endocarditis, according to the criteria which they have laid down for confirming their own case.

In addition to the above fourteen cases, the authors report these two of acute endocarditis, as described above. In neither case were blood cultures made before death, nor was the presence of endocarditis suspected. Death occurred on the thirteenth day and sixth day of illness respectively. In both cases the lesions of the lungs were found at autopsy to be very extensive, and it is to be considered that these were the direct cause of death.

It is of interest to note that in the first of the two patients mentioned above, the recent vegetations on the aortic cusps were found on a valve already injured, probably by syphilitic infection, and that in the second case the fresh lesions of the aortic valve were also engrafted upon the site of an old inflammatory process, although in this case there was also a vegetation on the mitral valve which revealed no evidence of previous disease.

Attention is called to the care necessary for the isolation of the organisms at autopsy. In the second case, culture from the heart's blood was negative. In the first case it was positive, but smears and cultures from the surface of the granulations gave a negative result, although the material from the center of the lesions yielded a pure culture and showed numerous bacilli, in direct smears.

**Pericarditis as a Complication in Pneumonia.** Records of 300 necropsies on pneumonia patients from the Medical Service of the United States Army Base Hospital at Fort Riley, Kansas, are the basis of this study. Among this number, pericarditis was found to have occurred in seventy-two, or 24 per cent. The report was

PLATE XIV.



Pericarditis following pneumonia  
fluid. Recovery.—Stone, page 344.

Three aspirations of serofibrinous

PLATE XV.



Purulent pericarditis with rotation of heart toward posterior chest wall, due to adhesive mediastinitis. Five aspirations. Recovery, but with marked disability.—Stone, page 344.

read by W. J. Stone<sup>s</sup> before the Section on the Practice of Medicine at the Seventieth Annual Session of the American Medical Association, June 19, 1919. The facts are carefully analyzed and clearly discussed.

The conditions seen in two of these patients by *x*-ray examinations are shown in Plates XIV and XV.

The following excellent summary brings out the points of interest and value in this paper:

Pericarditis was found to have occurred in seventy-two, or 24 per cent. of 300 patients, who succumbed to pneumonia. Acute purulent pericarditis occurred in 61.1 per cent. of the seventy-two instances; acute serofibrinous pericarditis in 19.4 per cent.; while the subacute fibrino-plastic and purulent form producing the "shaggy heart" occurred in 19.4 per cent. The quantity of pericardial fluid present in acute serofibrinous pericarditis varied from 250 to 1,000 c. c. With this form, pneumonia of both lungs was present in 50 per cent. of the patients, of the right lung alone in 28.6 per cent., and of the left lung alone in 21.4 per cent. In acute purulent pericarditis, the quantity of pus in the pericardium varied from 100 to 1,000 c. c. The average in twenty-six instances in which the amount was recorded was 350 c. c. Pneumonia involving both lungs had occurred in 47.7 per cent. of the cases, involving the left lung alone in 31.8 per cent., while in 20.4 per cent. the right lung was alone involved. In 54.5 per cent. of these instances, empyema of the left pleural cavity was present.

In the subacute form of fibrinoplastic and purulent pericarditis, producing the so-called "shaggy heart" pneumonia of both lungs had occurred in 35.7 per cent. of the cases, of the right lung in 35.7 per cent., and of the left lung in 28.6 per cent. Bilateral empyema had occurred in 35.7 per cent., of these instances, right empyema in 21.4 per cent., and left empyema in 28.6 per cent.

The type of infection isolated from the pericardial fluid corresponded generally to the type of infection isolated from the pleural fluid. In about 75 per cent. of the patients, streptococcus infection (usually one of the hemolytic varieties) was present.

The most important factor in the development of pericarditis appeared to be the occurrence of empyema. Pericarditis appeared to have resulted by contiguous extension from an empyema in many instances. Pericarditis and the associated myocardial changes were important contributory causes of death in empyema both prior to and subsequent to operation.

In the diagnosis of pericardial effusion in amounts varying from 300 to 500 c. c., the physical signs and the roentgenograms were fairly dependable, despite the extensive associated pathologic condition which confused the picture. In the diagnosis of smaller amounts (from 10 to 150 c. c.) of purulent material in the pericardium, the clinical signs were untrustworthy and the roentgenograms of little assistance.

Paracentesis of the pericardium was an important diagnostic and prognostic procedure. In acute serofibrinous pericarditis with large effusion, aspiration of the fluid was an important means of securing relief from the cardiac embarrassment.

The more radical procedure of incision and drainage of the pericardium in purulent pericarditis was not considered advisable in any of these patients, in whom the condition was suspected, because of the extensive associated pathologic condition.

**Actinomycosis of the Heart.** An example of this rare condition came under the observation of Letulle and Hufnagel.<sup>9</sup> Less than two dozen cases are known, and half of these were made up of suppurative metastatic emboli from foci of the ray-fungus in distant parts. In this case, there was invasion of the walls of the heart by contiguity of tissues, and some dozen similar instances are on record.

Actinomycosis of the esophagus propagated to heart and lung, and setting up extensive lesions of the pericardium, myocardium and endocardium (actinomycotic pancarditis): A man, aged 34, was admitted with intense dyspnea and general edema. Weakness was marked and some mental confusion rendered the examination extremely difficult. Pulse was very rapid; heart tones were muffled. Diagnosis: asystolia; death occurred on

(9) Bull. de l'acad. de méd., June 24, 1919.



the following day. Later, it was learned the affection began during the mobilization three years before. After drilling for some time, the man was sent to hospital for "pleuritis and bronchitis." After a stay of four months he rejoined his regiment. He had been ill ever since, but was able to work at intervals. He always coughed much and had difficult breathing, but never any expectoration. About two months before admission, progressive edema began to appear: the waistband of his trousers had to be enlarged, and the dyspnea and cough grew worse.

Necropsy showed that the invasion of the heart seemed to have followed two rather distinct routes: (*a*) Along the auriculo-ventricular groove posteriorly, projecting up under the much-thickened endocardium; (*b*) this was easily followed with the naked eye—the pericardial route, from above down and from behind forward, in the thickness of the myocardium of each ventricle; there the colonies pushed on step by step, invading successively the different layers of contractile fascicles.

Simultaneously, the actinomycotic mediastinitis opened up a still more accessible route for the fungus to the right pleura and base of the lung, the pleural symphysis and the vast patches of pulmonary sclerosis show the route, as far as the lumen of the bronchi corresponding to the affected pulmonary parenchyma.

Among the most interesting destructive lesions discovered by Letulle and Hufnagel in this case was the frequency of *actinomycotic phlebitis*. In the most typical areas there was specific panphlebitis. The nature and magnitude of the elastic alterations were remarkable, as was the rapidity of the atrophy in the muscular coat, and the fact the obliterating thrombi in the lumen were made up of pure leukocytes.

The arterial lesions seemed slower and more discrete, they resist the toxins from the actinomyces better; obliterative vegetating endarteritis always was found among the most common chronic alterations. But, in direct contact with an infective focus, all vessels—arteries, veins and lymphatics—are rapidly destroyed and may disappear without leaving any trace. In this re-

spect they follow the common law which provides that when the actinomyces pass through tissues and organs, all, no matter what their composition, are condemned to irremediable centrifugal destruction.

**Hydatid Cyst of Heart, with Secondary Echinococcus Infection of the Pericardium.** At the anatomic society (Paris) F. Dévé<sup>10</sup> narrated the case of a vigorous soldier who died suddenly. Necropsy disclosed coalescence of the pericardium, accompanied by multiple cysts of the heart: one of which had ruptured into the left auricle. There were no cysts in the liver or other viscera.

Study of the specimen showed secondary hydatid disease of the pericardium complicating a cyst in the myocardium of the left ventricle, with rupture into the serosa sometime previous. The cyst found open in the auricle was one of the pericardium itself developing in Theile's canal. In addition, the visceral pericardium showed small nodules of hydatid "pseudo-tuberculosis." Lastly, the aorta at the origin had an infundibulum adhering to a pericardial cyst on the way to involution. The histopathologic study of this proved it to be an old rupture of a subjacent cyst into the lumen of the aorta.

**Extensive Venous and Cardiac Thrombosis.** The study of a single patient constitutes the basis for this article, dealing with cardiac disease, with extensive venous and cardiac thrombosis.

The patient, a woman 39 years old, was in the service of F. G. Finley,<sup>1</sup> at the Montreal General Hospital. Five weeks previous to her admission there she was taken suddenly ill with rather severe pain in the right side with diminution of power in the right arm and leg. There was at the same time severe dyspnea, which became worse with cough, and pain in the chest, while the pain in the side lessened. As time went on the paralysis of the arm and leg became more marked, and facial paralysis on the opposite side developed. The maximum temperature at the time she was admitted was 104.8° F. The pulse was small, the blood-pressure 158, systolic, and 120 diastolic. The heart was found to be moderately enlarged, and there was a marked proto-diastolic gal-

(10) *Presse méd.*, Feb. 7, 1920.

(1) *Canadian Med. Ass'n Jour.*, October, 1919.

lop rhythm. A faint diastolic murmur was heard at the pulmonary cartilage.

Eleven days after the patient was admitted she complained of severe pain in the left forearm. During her illness there was considerable dyspnea, often orthopnea, with a moderate grade of cyanosis. The heart almost constantly presented the pre-systolic gallop rhythm and there was heard only an occasional systolic murmur at the apex, while the diastolic murmur heard on admission passed off soon after admission, being heard on only two occasions. There was increased blood-pressure until late in the disease.

The urine varied in specific gravity from 1021 to 1026, containing 0.6 to 0.9 per cent. of albumin, granular and hyaline casts, pus and epithelium. The daily quantity of urine varied from 150 to 600 c. c.

The Wassermann reaction on the blood was negative and the blood cultures on several occasions were negative. Electrocardiographic tracings were normal, and also the fundi of the eyes were unchanged.

The patient died and the anatomic diagnosis was as follows: Myocarditis, acute and chronic; endocarditis, acute; mural thrombi, multiple, in ventricles and right auricle; pulmonary infarcts; fibrous pleuritis; passive congestion of liver and kidneys; thrombosis of subclavian veins; thrombosis of pulmonary artery.

*Staphylococcus aureus* was found in the heart's blood at autopsy, in infarcts of the lungs, and in the softened cardiac thrombus in the left ventricle.

The presence of bacteria in the cardiac thrombus raises the question whether they are the cause or merely the secondary invaders of the clot. Cardiac thrombi are usually sterile, and form in marantic conditions, particularly when any localized area of degeneration is present in the heart wall. That these conditions were present in this case does not, however, enable one to exclude the possibility of a primary infection. Thrombi in veins are much more frequently associated with bacteria than are cardiac thrombi. In the case under discussion, the thrombosis was so widespread in the veins of the body that this condition must have been due to some cause acting in the blood itself, and although

it can not be positively stated that it was due to bacterial invasion, this seems to be the most probable hypothesis; and, if such a view is admitted it is logical to regard the cardiac clots as due to the same cause. The earliest clinical manifestation was the development of pulmonary infarction, and this may well have proved the starting point of the bacterial infection.

**The Energy Index of the Circulatory System.** A description of the energy index and its application to the study of the circulatory system is presented by J. H. Barach,<sup>2</sup> of Pittsburg.

He says that of all that has been said pertaining to the measurable functions of the circulatory system, there are three well-established facts: the systolic pressure, the diastolic pressure and the pulse-rate.

The author proposes an index which he calls the S. D. R. index, and which is based on these three known factors. For example, if in a given case the lifting force of the systole is 120 mm. of mercury and the diastolic force is equal to 80 mm. of mercury, then the force of the pulse beat which comprises both phases is 200 mm. of mercury. This, multiplied by the number of beats, indicates the total force per minute. He considers that neither the pulse rate nor the systolic pressure nor the diastolic pressure taken alone, gives sufficient information concerning the circulation.

He cites the effect of gravity, the effect of effort, and of reaction to epinephrine, on the circulatory system as indicated by the proposed index, and in each instance there is the expected increase. The index indicates the degree of activity of the circulatory system. It is not intended to measure the work of the heart, although it indicates that better than some of the formulas proposed for that purpose. It does not help to distinguish the cardiac load from over-load, nor cardiac strength from cardiac weakness, or velocity. It does indicate the amount of energy expended by the circulatory system in the performance of its function, and it gives information which is not obtained from any one or two elements in the triad upon which it is based.

Concerning the normal index, the author has found

(2) Arch. Int. Med., November, 1919.

that the upper limit is 20,000 mm. mercury pressure a minute. This was the figure obtained by examining young men from 18 to 30 years of age in civil life.

The energy index as found in the cardiovascular examination of men in the United States Army is referred to next. Of the 26,396 men examined in one period of forty-seven days, 1,171 questionable instances were picked out for special examination by the cardiovascular board of which the author was a member. These 1,171 men constituted all but the apparently perfectly normal ones of the series, including all who showed disturbances of rhythm, any abnormal sounds, prominent apex beats, abnormal pulsations, dyspnea, etc. Of these 1,171 men, 996 were finally accepted and 175 were rejected. Of the 175 rejects, 138, or 78 per cent., had an index of not more than 20,000. The final figures indicate that the S. D. R. index,\* as a guide to abnormalities in function of the cardiovascular system in this series of 26,396 men was correct in 99.95 per cent. In cases referred for special cardiovascular examination, that is, in the clinically doubtful cases, the S. D. R. index proved a correct guide in 78 per cent. It is stated again that the index does not indicate heart disease, nor decompensation nor physical stress. It designates the amount of effort which the circulatory system is putting forth at the time. The high index indicates increased cardiovascular effort in the action of the heart and blood-vessels, which is accelerated because of inability to accomplish their work at a normal rate of activity; or that they are fully capable of doing their work, but the resistance to their functioning is great. Either condition is pathologic and the variation of the index from the normal calls attention to this. A low index means either that the circulation is accomplished with little effort, or an inability to expend the necessary effort.

Minor changes in the circulation, such as are induced by the slightest alterations of the bodily functions, the effect of drugs, etc., may be detected by the S. D. R. index.

**Hypertension as Observed in One Hundred and Fifty Patients.** This discussion of hypertension by R. Cum-



mings<sup>3</sup> is based upon the study of 150 patients who presented the condition. Some of the terms or expressions which are used throughout the paper are defined first. For instance, apical abscesses are spoken of only when the *x*-rays have unquestionably demonstrated an abscess at the apex of one or more teeth. Bad teeth refer to very evident defects of the teeth, but which have not been shown by the *x*-ray. The statement of a positive history means that one or both parents died of apoplexy, uremia or heart failure. Moderate sclerosis refers to the radials, which when empty are palpable. Moderately severe sclerosis refers to the radials which are becoming tortuous; severe sclerosis to those becoming tortuous and beaded; while very severe designates a pipe-stem condition of the blood-vessels. By the term "nervous" is meant a group of patients with nervous temperament who are high-strung, intense, always keyed up to a high pitch, always "on the go," never relaxing, whose motors always run at high speed. This group does not know how to play, but are Rooseveltian in that they are intense in all they do, and a vacation means but a change to more strenuous work. These patients are always prompt in their appointments, are exacting, and in business very successful. The second group under this heading comprises women in the menopause period.

Of the 150 patients considered, 129 or 85 per cent., were between the ages of 40 and 70 years, eighty-four, or 56 per cent., were females, with fifty-six, or 44 per cent., males. One hundred and thirteen of the 150 belonged to the nervous group, forty-five of these being women in the menopause period; ninety-six of the 150 used no tobacco, while but two of the remaining gave a history of using it to excess. One hundred were total abstainers, and but three gave a history of liquor abuse. Sixteen patients were afflicted with over-eating and seventeen with obesity. Thirty-one, or 20 per cent., had apical abscesses and thirty-two had bad teeth. Chronic constipation was present in sixty-five, or 43 per cent.

The Wassermann test was done in fifty-two instances, being negative in all but one. Thirty-five patients had distinct signs of infected tonsils; it is not known that

PLATE XVI.



Case 1.—A mass of fine coiled wire found at necropsy in the ascending portion of an enormously dilated aortic arch.—Hare, page 356.



many more did not have this same condition. Urine examination was done in 136 cases, and a trace of albumin found in practically all; casts were present in but forty. Of fifty-seven subjects on whom the phthalein estimation was done, forty-three were normal and fourteen below normal. The blood nitrogen was estimated in forty-four, being above normal in but six.

To classify the series into those who have a primary nephritis hypertension, and those who have a hypertensive cardiovascular disease, according to Janeway's classification it is found that thirty belonged to the former group and 120 to the latter.

In the group of thirty patients whose increased pressure was due to kidney disease, there are included those with prostatic obstruction also. This leaves 120 or 80 per cent. of the subjects whose hypertension was due to causes other than renal disease. The group designated as being nervous numbers 113, or 75 per cent. Subtracting the forty-five who were in the period of the menopause still leaves 45 per cent. of the entire number of patients. In these the nervous symptoms greatly antedated the possibility of an increase in blood-pressure, so that the so-called nervousness can not be attributed to blood-pressure as the cause. These patients had either an increased vasomotor stimulus of central origin or a hypertensive substance in the blood.

With the group whose pressure arose during the period of the menopause, it is reasonable to suppose that the increased blood-pressure is a result of the things that cause the menopause, which is based on the change or partial cessation of ovarian function.

The fact that about 25 per cent. of all these patients had undoubted chronic tonsillar infection is of sufficient significance to consider this seriously from an etiologic standpoint.

Inasmuch as 41 per cent. of the whole number suffered from chronic constipation, this condition has a distinct bearing on hypertension. Splanchnic spasms seem the mode by which this condition operates. It is evident that in this group of patients syphilis played a very small part in producing hypertension.

Mention need hardly be made of the fact, that high

blood-pressure *per se* is not treated, but it is considered as a leading symptom, just as fever is a symptom in certain conditions.

Concerning results obtained by management, it seems the opinion of the author that more is accomplished in the nervous group than in any other. The treatment here must be based on the removal of the causes. Apical abscesses must be removed. Free bowel drainage must be instituted and maintained. All points of infection whether from the appendix, the gall-bladder, or the tonsils must be removed. A complete rest cure and if necessary a re-education of the patient's nervous system, from a nervous to a more phlegmatic temperament, must be undertaken. With this group bromides are the supreme vasodilators and one will find a lowering of blood-pressure in just the proportion of nervous relaxation obtained. Whether this medicine works by lessening nerve stimuli or sedating adrenal activity, or in neither of these ways is not known, but combined with rest it does work.

Excellent results are obtained with women in the menopause period. Almost constant complaint with these patients are general nervousness and hot flashes. Bromides, rest, and an empirical mixture of thyroids, ovarian and corpus luteum extracts will not only relieve the hot flashes but cause the blood-pressure to drop to the region indicated by the amount of vascular sclerosis and cardiac hypertrophy.

In conclusion Cummings points out that nephritis does not play so important a part in hypertension as was formerly believed.

There is a large group having increased blood-pressures who can be cured if seen early, and greatly relieved if seen later. All possible causes must be carefully searched out and radically treated. In addition, nervous habits must be changed, which in itself may mean the complete re-education of the patient. Too much emphasis cannot be placed upon insisting that a proper amount of rest and sleep be had.

Every woman should have the blood-pressure taken during the climacteric especially if hot flashes and nervousness are present. The marked relief of these symp-



toms by the use of bromides and internal secretory extracts, has been most gratifying.

**Blood-Pressure and Prognosis.** V. Topp<sup>4</sup> has investigated the subsequent fate of patients admitted to hospital with heart disease and high blood-pressure in the period 1913-16 inclusive. Of 164 patients with a permanently raised blood-pressure—that is over 180 mm. of mercury, there were 150 whose subsequent fate could be ascertained. Within two years 84 per cent were dead. The mortality rate was directly proportionate to the height of the blood-pressure. The expectation of life was the same for the two sexes (there were 118 men and thirty-nine women), and grouping the patients according to age brought out no difference in the prognosis for the various ages. Of the 16 per cent. who survived the two-year period, most were leading the restricted life of the chronic invalid. In two-thirds of all the cases, there were evidences of renal sclerosis but the mortality was practically the same for the patients with and without renal disease. The author criticizes Janeway's statements, made in 1913, and suggests that some fallacy must underlie his comparatively favorable prognosis in cases of high blood-pressure.

**The Prolonged Use of Cardiac Stimulants.** G. Galli<sup>5</sup> thinks that the use of cardiac stimulants can be grouped under three divisions: In the first group of cases, the drug is administered in large doses for a short period of time. Under this head we find young individuals affected with initial cardiac lesions. In the second group, the author classifies the chronic cardiopathies in which the drug is administered for a long period but in very small doses. The third group comprises those patients who have had an initial lesion but with transitory decompensation. The heart still retains a considerable reserve force. The administration of a few large doses to those cardiopaths is sufficient to bring about the desired result. Rest in bed for a short time is an indirect cardiac tonic. In other groups of cardiopaths there is more or less permanent change in the heart muscle, and continuous medication is necessary.

(4) *Hospitaltidn.*, June 4, 1919.

(5) *Presse méd.*, Jan. 27, 1919.

In mild cases 5 cgm. of digitalis is given in one dose once or twice a day, and this can be continued for periods of months. The tincture of strophanthus is commonly employed but its use varies considerably among internists. Gaston of Lyon suggests that the tincture of strophanthus be given in doses of 5 or 10 drops a day; strophanthus can be administered thus for from five to ten days without accumulative effects. The author cites the case of a peasant, 50 years of age, who took tincture of strophanthus for a period of two years at the end of which time he had a well-compensated heart and his only symptom was dyspnea due to cardiospasm. When the drug was discontinued the symptoms quickly subsided. The author also remarks on the large amounts of caffeine (10 to 15 cgm. of caffeine in a cup of coffee) taken in coffee by many individuals over a long period without any deleterious effects.

## ANEURYSM

**Aortic Aneurysm, Treated by Wiring and Electrolysis.** A study of three patients with aneurysm of the aorta is published by H. A. Hare<sup>6</sup> of Philadelphia.

The first patient considered was a man about 40 years old, who, when examined, was found to have a very large aneurysm, involving the entire arch, but pointing anteriorly as shown in Figure 13. Eight feet of wire were passed into this aneurysm, and the current passed through the wire for thirty minutes, the maximum being 35 milliamperes. Great pain was completely relieved in one hour. Twelve days later, an extension of the bulging having occurred on the left, a second operation was performed in which sixteen feet of wire were put into the aneurysm to avoid the tendency to rupture and in order to relieve pain caused by the new source of pressure. This man died one month after his first operation, the cause of death being pulmonary edema. Necropsy revealed an enormously dilated aortic arch in the ascending portion of which a mass of fine coiled wire was found surrounded by blood clots (Plate XVI).

The second patient studied was a man of 42, who pre-

(6) Jour. Amer. Med. Ass'n, Dec. 20, 1919.

sented a very large aneurysm of the descending arch, pointing anterolaterally as shown in Figure 14. This mass measured 14 inches from below upward and 12 inches transversely. Eighteen feet of wire were introduced into the aneurysm and the current was passed for one hour and 11 minutes, the strongest being 40 milliamperes, continued for eleven minutes. The patient



Fig. 13 (Case 1). Aneurysmal growth, 10 inches in width and 8 inches from below upward.

improved, but died one month after the operation from internal rupture of the aneurysm.

The third patient was an iron worker, 50 years old, who presented an aneurysm of the ascending arch about  $2\frac{1}{2}$  to 3 inches in diameter, rather sharply defined and sacculated. Twenty feet of wire were passed into the aneurysm and the current passed through the wire for 40 minutes, the greatest strength being 46 milliamperes. This patient was also relieved of pain very promptly. Ten weeks after operation, the man was urging that he

be allowed to go back to work, and only a very faint impulse could be felt in the spot involved.

Hare points out that there are several points essential to the success of this method, and a number of others which, when understood clearly, show why it can not always succeed:

The aneurysm must be sacculated, not fusiform, and if it be of the dissecting sacculated type it is the most favorable for good results. It is not only useless but dan-



Fig. 14 (Case 2). A large aneurysm of the descending arch pointing anterolaterally and measuring 14 inches from below upward and 12 inches transversely.

gerous for obvious reason to operate on a fusiform aneurysm.

Although it is not at all necessary for the aneurysm to have eroded the chest wall so as to protrude, it must be close enough to the chest wall anteriorly or posteriorly to permit the insulated needle to enter the sac.

The wire must be of gold and platinum so that it will coil properly in the sac. A gold-copper wire is useless because the copper is eaten out so rapidly by electrolytic action that the procedure can not be completed.

Great care must be taken that the skin over the sac is protected from electrolytic action by having the external part of the needle well insulated as well as the shank.

Depending on the size of the sac, the amount of wire varies, but usually from 15 to 20 feet are required.

The time during which the current is allowed to pass is usually about forty-five minutes, and the current must be turned on and off very gradually.

If the street current is used, great care must be taken that the proper reducing apparatus is employed, and also that the table on which the patient lies is insulated with rubber pads and that the operator and his assistant wear rubber-soled shoes.

The facts that stand in the way of complete success are that in a large proportion of cases the entire aortic wall is diseased, the area operated on being chiefly in trouble. Solidifying the contents of the sac is well so far as it goes, but other parts of the aortic wall give way later. In many cases the entire arterial system is diseased, and the only patient seen by the author, who did not get relief from pain before the operation was finished died suddenly sometime later and the necropsy revealed a second sacculated aneurysm, just above the diaphragm, which had ruptured.

The best results so far achieved in patients of this kind treated by Hare have been in the case of a man who lived in comfort for three years although threatened with pulmonary edema when operated on. He did not die of the aneurysm but was killed by a freight train.

## AORTIC DISEASE

**Syphilitic Aortitis.** The subject of syphilitic aortitis and its early recognition is presented by G. E. Brown,<sup>7</sup> who says that this type of aortitis is very common when diagnosed on the autopsy table, but rare when reviewing clinical reports. This discrepancy may be explained in several ways:

First, aortitis is often a latent manifestation of syphilis; second, signs and symptoms of its presence are either lacking or so insignificant as to be entirely overlooked; and third, the medical profession has not given this condition sufficient attention, and careful examination of the aorta is slighted or else entirely ignored.

Brown refers to the statistics of Gruber, who by an examination of 6,000 autopsy records found a diagnosis

(7) Amer. Jour. Med. Sci., January, 1919.



of luetic aortitis in 4 per cent. of them. Marchand has reported 256 autopsies on bodies with acquired syphilis, in 82 per cent. of which luetic aortitis was found. Obendorfer found in 1,436 autopsies on adult bodies that 7 per cent. showed aortic lues, and in forty of these the diagnosis was made by the autopsy findings.

In a group of 136 cases of syphilitic aortitis, Goldscheider found tabes in twenty-nine. Other investigations show aortitis in from 30 to 40 per cent. of all cases of tabes and general paresis.

In the routine use of the Wassermann reaction in Brown's work, he found seven cases of specific aortitis in 136 positive Wassermanns, or luetin tests of 5.1 per cent.

Microscopic examination of an aorta that is infected with the *Spirochæta pallida* shows that all three coats of the arterial wall are involved, the invasion taking place through the vasa vasorum. The adventitia is attacked first, then the media, and these coats bear the brunt of the damage. Collections of lymphoid and plasma cells are found and occasionally giant cells. These occlude the vasa, with resulting weakening of the middle coat. This yielding of the media shows itself later as saccules, bulgings and aneurysms. The cellular collections may show as nodular masses on the intima.

The gross lesions are characterized by irregular folds and roughenings of the intima—translucent and pearly plaques. These cushions or wheels may be yellow in color. The distinction between atheromatous deposits and luetic changes is found in the absence of fat and calcareous deposits. The two conditions are frequently coincident. Syphilis usually attacks the aorta at its orifice, and when the extension is toward the heart the valves and coronaries usually suffer, with disastrous consequences to this organ. The extension may be from the heart, and in this group of cases the damage is usually less severe. No portion of the thoracic aorta is exempt.

Rarely is the abdominal aorta invaded. The gross pathologic picture includes the characteristic wrinkling of the intima—longitudinal rugae, thinned out and scarred areas. The more advanced stages are shown by small saccules and aneurysms.

Syphilis of the aorta is classified, according to Dieulafoy, as follows:

When the disease is confined to the first portion of the aorta—suprasigmoid aortitis.

Syphilis of the aortic valves with incompetence.

Aneurysmal forms.

Obliteration of the coronary vessels.

Brown thinks that physicians are not sufficiently acquainted with the earlier form of luetic aortitis in which the disease has not advanced to a stage where the gross changes are easily detected and where careful examination shows no aortic valve lesions. The symptoms are extremely indefinite at this stage and are not clear cut. Often they are not severe enough to alarm the patient, but the fact that chest symptoms are generally associated in the mind of the laity with tuberculosis, often brings these patients to the physician with a request for a chest examination.

The first symptom is pain. This is the most frequent symptom, and its characteristics are that it originates under the sternum, that it produces a sense of constriction or compression, that it radiates into the brachial plexus, with the characteristic arm localization, usually of the left side and rarely of the right side, and very rarely both sides.

Of the indefinite symptoms that are complained of the first is fatigue. The patient usually is weak, neurasthenic, becomes tired easily, suffers from mental fatigue, and mental disturbances and headaches. Dyspnea is also an important symptom and was present in all cases seen by the author.

Hoarseness is usually associated with pressure on the recurrent laryngeal nerve. Fever may be present in certain instances. Cough may be present, and this is usually dry and non-productive. Cyanosis is often observed.

In the early stages of luetic aortitis, any one or more of these symptoms may be present. Of first importance among the physical signs that indicate this condition, are the alterations in width and contour of the aorta. The Roentgen diagnosis is by far the most satisfactory method for demonstrating changes in the aortic arch. Roentgen

rays show one or more of the following changes in the normal aortic curve: Enlargement of the aortic shadow to the right; enlargement to the left, with obliteration of the normal aortic knob; enlargement both to right and left; increasing density of the aortic shadow is suggestive, as is also reduction of the aortic pulsation when viewed fluoroscopically.

Other signs of doubtful value as palpitation of the aorta in the jugular notch, elevation of the subclavian arteries, undue mobility of the apex due to elongation of the aorta, and a clanging second sound during the heart cycle. Blood-pressure as a rule is not elevated in this condition. The aorta should be examined both fluoroscopically and with plates. About 75 per cent. of specific aortitis cases show a positive Wassermann reaction, and a certain percentage of the balance will show a typical luetin test. The presence of a positive Wassermann reaction in the absence of any signs of syphilis should direct attention to the aorta, and in many cases an early aortitis will either be found or suspected and treatment instituted early enough to forestall the more serious symptoms, which are sure to follow.

The final important corroborative evidence is the therapeutic test, and when a group of symptoms clears up under a course of mercury and iodides or an injection of salvarsan, a suspicious case becomes a diagnostic certainty and treatment is instituted with the assurance of a permanent improvement or perhaps a cure.

**Aortic Disease in Soldiers.** Observations on aortic disease by T. F. Cotton,<sup>8</sup> in a study of fifty soldiers with signs of aortic insufficiency are recorded.

By the symptoms alone, aortic disease is divided in this study into three types: First, aortic disease without symptoms; second, aortic disease with a group of symptoms which are termed "the effort syndrome"; third, aortic disease with venous engorgement or angina pectoris.

With the first type there are no symptoms, and the condition is recognized by the signs alone. Fully developed incompetence of the aortic valves is compatible with good exercise tolerance: the severest form of exer-

(8) *Lancet*, Sept. 13, 1919.

cise can be performed without greater distress than that observed in a healthy untrained subject. The extra load put on the heart by the reflux of blood through the defective valve is cared for by the large reserve power which a healthy or slightly damaged myocardium possesses. Not until the cardiac muscle has been sufficiently impaired—for example, through coronary or myocardial disease—does the heart fail to bear the extra work put upon it, and with the exhaustion of its reserve give rise to the symptoms of heart failure. The uncomplicated valvular defect, the simple crumpling of the aortic cusps, is not in itself of great consequence. The reason that in so many cases aortic disease leads to heart failure is that the coronary arteries, or the myocardium, or both, have been damaged by the same agent that has caused the valve defect.

The second type presents the effort-syndrome group of symptoms. Breathlessness on exertion is always present; this respiratory distress is provoked by an effort which, in a healthy person, would not be complained of. It is absent at rest save in rare instances. Occasionally it is noticed at night in bed, and is described as a choking sensation, a feeling of suffocation; it is sudden in onset and of short duration. This is not to be confused with the nocturnal breathlessness due to deficient aëration of the lungs, nor the paroxysmal dyspnea of relative acidosis in cardiorenal disease. It is frequently encountered in the effort syndrome case in which there are no signs of structural disease. Palpitation is a common complaint. When provoked by exercise it is felt after the effort; it is associated with an over-acting heart and persists as long as the excessive heart-ache is maintained. Emotional stimuli, excitement, fear, pain, joy, etc., give rise to the same symptoms. Briefly, the symptoms in D. A. H., so-called, and in the aortic cases are identical, indistinguishable, the one from the other. The symptoms in aortic disease arise from a variety of causes. They appear in large number after an acute infection—after rheumatic fever, pneumonia, bronchitis, trench fever, malaria and dysentery. In others, gas poisoning, shell shock, severe effort, are at least associated with the

cause. In others, the symptoms are gradual in onset and can not be associated with any particular cause.

Aortic disease of the third type, when there is venous engorgement or angina pectoris is briefly discussed. The symptoms here are not those of aortic regurgitation, but those of heart failure, with venous engorgement. There are the symptoms of venous stasis in the pulmonary circulation on the one hand, cyanosis, orthopnea, and pulmonary congestion; and on the other the symptoms arising from the failure of the heart to maintain the general circulation, edema of the extremities, general anasarca with disturbance of the renal and other abdominal visceral functions, cerebral manifestations, and the final moribund state of the human organisms.

The prognosis in aortic disease depends on so many different factors that it is very difficult to make, and at best, is most uncertain. The degree of involvement of the aortic valve, the coronary arteries and the heart muscle, are prominent factors in determining this question.

**Rupture of Abdominal Aorta.** In the case under observation by Devic and Lamy,<sup>9</sup> a man of 53, was admitted to hospital with extremely violent crises of pain in the abdomen and the lumbar region and radiating to the groins. There were no stigmata of syphilis, the vascular system was entirely normal, and signs of incipient tabes were absent. Lumbar puncture evacuated cerebrospinal fluid under high pressure with lymphocytosis. The painful attacks recurred often during three weeks, and one night death ensued suddenly without cry or struggle.

Necropsy disclosed an enormous recent clot occupying all the subperitoneal connective tissue. On the posterior surface of the aorta, midway between the celiac axis and the division into the iliaes, was a transverse rupture at the site of a patch of atheroma. The rupture had occurred on two occasions, and a false aneurysm the size of a small orange, had begun to form, then the second rupture proved fatal. The remainder of the course of the vessel was studded with many plaques of atheroma.

(9) Presse méd., Dec. 17, 1919.



Other organs were negative. Histologic examination showed the undoubted syphilitic nature of the lesions, in spite of the absence of antecedents. The violent attacks of pain can be explained by irritation of the solar plexus.

## ANGINA PECTORIS

**Angina Pectoris.** In an address on this subject, H. C. Gordinier,<sup>10</sup> gives first an historical account of the disease. He states that to Heberden belongs the honor of first directing attention to the complex of symptoms which he named angina pectoris. In his first communication, read July 21, 1768, Heberden published his experience, spread over more than twenty years, which contained a most accurate account of the symptoms and postmortem findings.

Concerning the pathology, the inorganic or functional type shows no naked-eye changes and probably has for its cause sudden increased intra-aortic pressure from general vasomotor spasms. The common autopsy findings in bodies that have died from this condition is disease of the beginning of the aorta at its root, about the sinuses of Valsalva, aortic valve disease, luetic mes-aortitis, or aortitis due to acute infection, atheroma, atherosclerosis, often comprising the origin of the coronaries, general sclerosis of the coronaries, with remarkable thickening and tortuosity with partial or complete obliteration of their caliber, with or without calcification and, not rarely, thrombic formation. It must be remembered, however, that thickened tortuous sclerotic coronaries which are often exceedingly narrow, are frequently found at autopsy in patients who have never suffered from angina. On the other hand, a number of sufferers have died of angina, whose coronary arteries were found patent and otherwise normal.

Gordinier thinks that perhaps the most frequent association with angina pectoris is syphilitic aortitis, a true mesaortitis due to primary changes, endarteritis of the vasa vasorum. The myocardium shows degenerative changes characteristic of syphilis in many cases.

<sup>(10)</sup> Med. Record, Oct. 4, 1919.

As to etiology, the condition occurs most commonly in adults between the ages of 45 and 65 years, but it has been seen in many instances in children between the ages of 7 and 15.

Osler is quoted as finding among 268 patients, thirty who were under 9 years of age, forty between 30 and 40 years, fifty-nine between 40 and 50 years; eighty-one between 50 and 60, sixty-two between 60 and 70 years, thirteen between 70 and 80 years, and three above 80 years.

Heredity undoubtedly exerts a prominent influence in the evolution of this complex of symptoms. Women are much less frequently affected with true angina than are men. The acute infectious diseases, more notably acute rheumatic and scarlet fever, grippe, typhoid fever, variola, diphtheria, and septic infections, predispose to angina because of the not infrequent complication of infectious aortitis.

Of all causes, syphilis stands preeminent. It is doubtless the most common and is the causal factor, either hereditary or acquired, in many of the earlier and most of the cases of middle life, and not a few cases in later life.

Metabolic and chemical toxins, such as occur in gout, diabetes, and plumbism, are etiologic factors. The pressor effects of over-indulgence in tobacco is in the author's opinion frequently the exciting cause of an attack. Alcohol probably plays a definite rôle, although the studies of Cabot seem not to favor such an opinion. Of the immediate exciting causes, sudden increase of blood-pressure occasioned by mental worry, sudden grief, great strenuousness, that is, bodily labor strain, rapid walking especially against a resistance, such as the ascent of a hill, hurrying upstairs, running to catch a train, heavy lifting, leaning over to button the shoes, facing a strong wind, sudden exposure to intense cold, straining at stool, and heavy eating followed by exertion, especially at night, are among the more important.

In describing the symptoms, pain is put forward as the great subjective feature of an attack of angina. The other symptoms are simply grouped around it. The pain may come on so abruptly and be of such an intense

agonizing character that fatal syncope occurs almost immediately. Death in such cases is probably due to complete vagus inhibition. The attacks both of angina minor and major are nearly always preceded by some unusual mental or physical strenuousness, or play the part of the so-called attack of indigestion, or follow emotional excitation. They are paroxysmal in nature, but may occur so frequently as to produce the condition known as "status anginosus."

Over the region in which the subjective sensation of pain is experienced, there is nearly always hyperesthesia and tenderness along the course of the vessel walls.

Concerning angina abdominalis, the author cites the record of a single patient of his, a woman, 60 years of age, with hypertension and an enlarged heart with a ringing aortic sound. Tracings showed no alterations. Her pulse was regular, 68 a minute. She had had a few days previously a very severe pain of a constricting character, beginning in the middle of the abdomen and radiating into the sternum and into the left shoulder. She thought she would die in the attack. Nitroglycerine relieved the paroxysm, and *angina abdominalis et pectoris* was diagnosed. These cases are cited as examples *par excellence* of those that are often unluckily diagnosed as indigestion, gastric ulcer, gall-stone disease, appendicitis, pancreatitis, etc., and not so rarely submitted to unnecessary surgical intervention.

Unless associated respiratory disease is present, breathing in angina is very little disturbed during the attack. There is rarely distinct air hunger. The respiratory movements may be fewer in number and the patient often instinctively fails to breath fully and deeply for fear of increasing the heart pang. In some cases the respirations are increased in number. Cheynes-Stokes respiration is generally a fatal sign.

During the attack, the patient usually assumes a fixed attitude, sitting or standing, with the trunk bent forward, and the head more or less fixed. The pulse in many cases of angina pectoris remains throughout the paroxysms perfectly regular in rhythm, not at all or slightly accelerated; frequently it is slower than normal.

Sometimes, however, the pulse is rapid, irregular in rhythm, feeble in volume and easily compressed.

If the attacks become complicated by occlusion of the larger branches of the coronary arteries, then the pulse becomes rapid, irregular, easily compressed; with a sudden fall of systolic blood-pressure, sustained diastolic pressure and symptoms of myocardial insufficiency are developed. The systolic pressure at the onset of the attack, nearly always rises beyond the normal level found in the interval between the paroxysm. The blood-pressure, however, is by no means always high. It may remain normal, or even drop below normal.

True angina may simply be subdivided into minor and major attacks. The term "pseudo-angina pectoris" should be excluded, Gordinier thinks, from the classification of the anginas. It merely indicates a lack of careful differentiation.

Of the theories offered for the causation of pain in this condition, that held by Sir Clifford Allbutt is in the opinion of the author the most rational so far presented. Briefly, it is as follows:

With the onset of an attack of angina pectoris there is a sudden rise in the intra-aortic pressure with sudden aortic distention which causes an irritation of the sensory terminal end-organs located in the suprasigmoid part of the aorta, thus exciting both the local and referred pain of the angina pectoris. This portion of the thoracic aorta is likened to a sensitive tambour regulating cardiac energy by the intermediation of the vagus, and it is diseases of this particular area that are most prone to be associated with anginoid attacks. Allbutt also states that he has never failed to find in a case of unmistakable angina, regardless of the state of the coronaries, disease of the suprasigmoid part of the aortic arch.

The mortality in this condition is of necessity very high. Death is not so rarely due to coronary arterial thrombosis; it may be sudden or it may occur after several days of suffering.

The cases due to tobacco, alcohol, gout, diabetes, and other metabolic toxins usually cease with the elimination of the toxins incident to them. The prognosis is espe-

cially favorable in a large number of cases, if early recognized, having their origin in syphilitic changes of the aorta-coronary area "suprasigmoid aortitis." Intensive and long-continued antiluetic treatment often cures.

In considering treatment the physician should be familiar with the condition of the myocardium, the cardiac reserve, the condition of the vessels and the blood-pressure, the renal functioning, the condition of the gastro-enteric tract, the amount of sleep, the exact character and amount of work, whether physical or mental, the habits of the patient as to excesses in eating, drinking and smoking, and the presence of any constitutional disease or vice which predisposes to angina, such as gout, diabetes or nephritis. He should be fully conversant with the character and frequency of the attacks and whether they are the mild or major type. A Wassermann reaction should be carried out in each case. The patient should be urged to eat sparingly, and warned never to exercise immediately after eating a meal, or to eat heartily at night, and the use of tobacco should be limited or absolutely prohibited. He should have the maximum amount of rest with freedom from worry and anxiety. Exercise should be limited to moderate walking on the flat, short of producing precordial distress, dyspnea or fatigue. Carriage or automobile riding is permissible. If possible the winters should be spent in the South.

The author states that for the paroxysms, the nitrites are almost specific, and at the onset he uses inhalations of amyl nitrite, to be quickly followed by good stiff doses of nitroglycerine, a 1 per cent. alcoholic solution dropped just beneath the point of the tongue in the sublingual region being used.

If relief does not speedily come from the nitrites, then recourse should at once be had to morphine and atropine. This latter drug will also help to stave off vagus inhibition. Additional doses of atropine should always be used in faintness, marked slowness of the pulse or if an intense feeling of impending death should come on, for it is generally believed that those sensations are in part or wholly due to vagus inhibition. Atropine dilates the peripheral vessels and probably the coronaries. Chloro-



form inhalations sometimes may give the only relief in severe anginoid paroxysms.

Cases of angina associated with or followed by myocardial insufficiency, particularly those cases associated with auricular fibrillation, flutter, or alternation, should receive digitalis until relieved and then be treated for long periods of time with small tonic doses.

The iodides, administered for long periods of time, are of unquestionable value in the treatment.

## DISEASES OF THE BLOOD AND BLOOD-MAKING ORGANS

**Cause of the Reactions Following Transfusion of Citrated Blood.** In discussing the cause of reactions following the transfusion of citrated blood, C. K. Drinker and H. H. Brittingham,<sup>1</sup> of Boston, say that in analyzing these reactions that follow any of the different methods now in vogue, all figures should be based on tables in which donor and recipient have been properly matched prior to the operation. By means of the methods of grouping and direct matching given by Moss and others, it is possible to exclude a certain number of gross hemolytic reactions which formerly were inevitable.

In spite of the apparent reliability of the best methods for matching donor and recipient, however, evidence steadily accumulates to the effect that these *in vitro* reactions are occasionally wrong.

In patients in whom many transfusions have had to be done it has been observed that it is more and more difficult to find donors whose blood will match that of the patient. A donor may match perfectly early in the series of transfusions but later be found unsuitable. This is probably due to the development of isohemolysins. It is, therefore, most important that the blood be matched before each transfusion.

The authors state that their experience with transfusion with the citrate method gives a larger number of reactions than are reported elsewhere. Out of eighty-three transfusions, the authors noted a rise in temperature of 2.5 degrees fifty times or 60 per cent., and of this number thirty-nine patients, or 47 per cent., had chills. These figures include all the transfusions of whole citrated blood which were done by different individuals at the Peter Bent Brigham Hospital.

In order to test the matter further the authors did seventeen such transfusions with the most extreme care to reduce the reaction percentage. In these transfusions

---

(1) Archiv. Int. Med., February, 1919.

there were nine rises in temperature above 2.5 degrees, or 53.3 per cent. and seven chills, or 40 per cent.

In describing the technique of transfusion and plan of observing the patient following the transfusion, they say that it was their custom to take temperature, pulse and respiration at the time of transfusion, and at half-hour intervals until the temperature had returned to its original level, or given positive indications of soon reaching it. For routine work such close following as this is unnecessary, but for analyzing reactions it is imperative and will disclose many unsuspected increases in temperature.

In describing methods of transfusing and handling blood they refer to having used four different specimens of sodium citrate derived from various sources without any variations in the result that could be attributed to the salts. As to the citration a variety of methods were used and none of them was found to have reduced the number of reactions. The cleanest and best is described as follows:

A one liter Florence flask indicated in Figure 15, containing 35 c.c. of 8 per cent. sodium citrate, is stoppered with gauze and autoclaved for fifteen minutes at 15 pounds. This does not alter the reaction of the citrate or its ability to prevent coagulation. The rubber stopper (B) carrying two glass tubes is boiled, together with a No. 19 needle, and the rubber tubes E and F. These deliver blood to the flask and should not be more than 5 inches long since it is desirable to eliminate as much contact of blood and rubber as is possible. This allows the operator to exert suction. This apparatus avoids stirring the blood and contact with the air. It delivers the blood through the long glass tube directly into the citrate without dripping slowly down the sides of the flask and the suction facilitates collection very markedly. Thirty-five cubic centimeters of 8 per cent. sodium citrate should keep fluid, 1400 c.c. of blood. It gives the patient 2.8 gm. of citrate, a dose far below the dangerous limit. Such citration insures a strength great enough to restrain coagulation in the 800 or 900 c.c. of blood ordinarily withdrawn, and after repeated observation it has been found to cause no hemolysis within three

hours' time. Citration has also been accomplished by using 2.5 per cent. of citrate in specially distilled water in the proportion of 10 c.c. to 90 c.c. of blood, and a 2 per cent. solution in the same proportion. These alterations do not change the frequency of reaction occurrence. Transfusion in this work varied in amount from 250 to 950 c.c. No definite connection has been observed be-

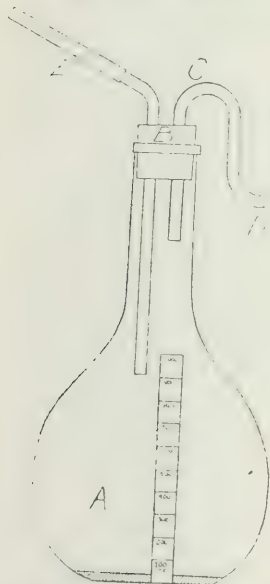


Fig. 15. Collecting flask containing sodium citrate solution.



Fig. 16. Injecting flask.

tween the amount of transfusion and the extent or frequency of reaction.

The injection apparatus is indicated in Figure 16. A fine needle (21) is thrust into the recipient's vein and with blood flowing freely connection can be made and the donor's blood driven in. The blood is filtered as it is transferred from the collecting flask to the injection apparatus, and for this purpose an old fine mesh, sterile towel is placed in the neck of the injection flask.

In attempting to determine what factor causes the

reaction in patients who are transfused in this manner a number of questions arose:

The first one was whether the cause of the reaction resides in cells or in plasma. Thirty transfusions were done taking the blood into citrate, centrifugalization slowly for five minutes, removing the plasma and washing twice. At the termination of the last two centrifugalizations carried on at highest speed, all "buffy" material was removed from the red cells. Such technique reduces the white cell count below half and plates are found with the greatest difficulty. It is impossible to consider such preparations plate-free, but the number of plates left is certainly exceedingly small. In this series, eleven persons, or 40 per cent., had the 2.5 degree rise in temperature and six, or 20 per cent., had chills.

The next question that arose was whether or not the reaction was due to some unsuspected factor, against which the donors were not tested.

In an effort to answer this question, transfusions were carried out by discarding plasma from the donor's blood, and washing the entire cellular contents four times and then bringing it to its original volume by diluting with physiologic and saline solutions, and injecting this into the person from whom the blood was drawn. Characteristic reactions were obtained in this way. Out of six instances of washed, whole cell content injections, six chills and pronounced febrile reactions all well above 2.5 degrees were observed.

Plasmapheresis, that is returning of the blood cells to the individual from whom they were taken, was done in patients with chronic nephritis eighteen times, taking the blood in citrate, washing twice, and returning the red cells freed as far as possible from plates and leukocytes. The technique corresponds exactly with that used in the transfusion of washed red cells of citrated blood. Not one of these patients had a chill or rise in temperature of 2.5 degrees. The majority reacted slightly and in four instances there was a rise above two degrees. All of these patients had advanced chronic nephritis, and while such individuals may be less reactive than the anemic patients, making up the bulk of the patients in this work, the results would seem to indicate that the



handling of perfectly compatible red cells with minimal exposure to citrate does not induce alterations of marked grade.

The third question encountered in this investigation had to do with whether citration altered the erythrocytes so as to render them more susceptible to hemolysis when injected.

In fifteen instances, blood was taken from donors into the ordinary collecting flasks mentioned above and defibrinated at once by shaking with glass beads. This removes all the plates and reduces the white cell count to about one-third. The red cells were centrifugalized off, washed twice, brought up to the original volume with physiologic sodium chloride solution and injected. These transfusions gave three, or 20 per cent., reactions of 2.5 degrees with one chill, decidedly better figures than were obtained by an citrated transfusion. They are contrasted with nine transfusions in which all procedures were identical except that 25 or 35 c.c. of 8 per cent. sodium citrate were added to the final red cell suspension one or two hours before injection. In these cases there were four or 44 per cent. reactions above 2.5 degrees, with two chills. It would thus seem that the mere addition of a normal dose of citrate to red cells develops slight abnormality.

In the discussion of this work it is said that if the plates are considered as removed from citrated blood by differential centrifugalization it is evident that red cells exposed to citrate in collection are more apt to cause reactions than those taken from fibrinated blood and subjected to the comparable amount of washing, 40 per cent. of reactions occurring in the first case and 20 per cent. in the second. If to these last cells citrate is added as the single difference in their treatment the reactions again become 44 per cent. Citration, therefore, seems to harm red cells and possible direct evidence for this exists in the occasional promotion of fragility by the substance. The indication is that the hemolysis contributes a certain number of reactions, but this hemolysis is too slight to be detected by direct methods.

It is concluded, therefore, that while the total of the different types of transfusion which were employed in

this work are not large, it appears that three elements make up the final total of reactions in citrate transfusions: (a) very rare gross incompatibility which escapes *in vitro* detection, (b) changes in the plates, part of the process of coagulation, and (c) direct action of the sodium citrate on red cells promoting hemolysis.

**Changes in the Blood Immediately Following Transfusion.** A study of these changes has been made by J. G. Huck,<sup>2</sup> of the Medical Department of the Johns Hopkins University and Hospital.

The object of the work was to find a clear explanation for the various changes that follow the introduction into one individual of the blood of another. Some of the simplest questions raised by this procedure remained unanswered.

The methods used consisted of transfusion in each instance by a modification of the citrate method of Lewisohn, as described by Sydenstricker, Rivers and Mason. Especial care was taken in testing the donors to be certain that the blood was compatible. The amounts of blood given in different cases varied from 250 c.c. to 1250 c.c. Studies of the blood were made immediately before the injection, immediately after the injection, two hours, five hours, and twenty-four hours later. These time intervals were followed rather closely in practically all of the cases. Each examination consisted of counts of the red cells and of the white cells, with a differential count of 300 white cells. Platelets were estimated in the smears and the hemoglobin was determined. Notes were also made on the morphology of the blood cells. Counts were always made with the same instruments and by the same observer, with the same reagents; and care was taken to draw the blood from the same part of the body, with uniform punctures.

The effect of the transfusion was studied in seven cases of pernicious anemia, two cases of idiopathic purpura, four of benzol poisoning, five of secondary anemia, and two of Banti's disease.

The responses to transfusion were found to be so variable that detailed protocols of the various patients are

---

(2) Bull. Johns Hopkins Hosp., March, 1919.

attached to the original article. The main points brought out may be summarized briefly:

Concerning the red blood cells, in general following the injection of blood there was an immediate increase in the red blood cells, the striking point being the marked increase in many cases apparently out of proportion to the quantity of blood introduced. Red cell counts rose in certain instances from 880,000 to 1,488,000 immediately after the injection of 500 c.c. and from 480,000 to 1,300,000 following the injection of 650 c.c. The hemoglobin in most instances showed a uniform rise following transfusion, usually reaching its maximum at the end of twenty-four hours, in some instances the hemoglobin fell slightly after the initial rise. Changes in hemoglobin did not run parallel with the changes in the red count as was seen best from the variations in the color index. In practically every case following transfusion there was some increase in leukocytes. In several instances, however, the leukocyte count remained practically stationary or even fell.

By way of discussion the author says that a general review of the immediate effect of transfusion upon the blood count in twenty cases does not reveal any constant changes following this procedure. The point of practical interest and importance seems to be that no exact mechanical effect can be demonstrated following the introduction of definite quantities of blood.

Whereas in a general way it may be said that the introduction of blood raises the count, the effect is essentially a biologic one involving the redistribution of blood in the body and its exact nature is not understood.

**Indications for and Results of Transfusion.** Before taking up the subject of the application of transfusion to certain diseases, E. C. Levine,<sup>3</sup> of Montreal, outlines briefly the history of transfusion. This part of his paper is omitted from the present abstract. He presents the following tabulation of results obtained in fifty-four direct transfusions in conditions indicated in the table.

---

(3) Canadian Med. Ass'n Jour., January, 1920.

## DIRECT TRANSFUSION METHOD

	No. of Cases		Results
Pernicious anemia .....	27	Temporary benefit .....	25
Hemorrhage .....	4	Rendered operation of	
Septicemia .....	5	splenectomy practicable..	2
Postoperative hemorrhage		Improved .....	4
(gall-bladder) .....	3	Improved .....	2
Gastric ulcer (hemorrhage)..	3	Not improved .....	3
Puerperal septicemia .....	2	Markedly improved .....	3
Hemophilia .....	2	Markedly improved .....	3
Pulmonary hemorrhage (T.		Improved .....	1
B. C.) .....	1	Improved .....	2
Postoperative shock .....	3	Improved .....	1
Typhoid perforation .....	1	Slight improvement .....	3
		No improvement .....	1

## SODIUM CITRATE METHOD

Pernicious anemia .....	3	No improvement .....	3
-------------------------	---	----------------------	---

It is noted that very little permanent good was achieved in the administration of blood in cases of pernicious anemia. Transfusion in such cases appears to have a temporary beneficial effect, which soon disappears and the patient returns to the previous state.

When splenectomy is to be done, transfusion of blood prior to the operation is found to be of benefit in sustaining the strength of the patient. In considering general indications for blood transfusion, the author names all conditions of depleted blood-supply, especially when operative measures are contemplated. This fact was very forcibly brought out in the treatment of wounds on the field of battle.

Under the heading of specific indications for blood transfusion, there are named, hemorrhage, primary and secondary; hemophilia; sepsis; typhoid perforation; puerperal septicemia; gall-bladder conditions with jaundice; gastric ulcer (hemorrhage, postoperative bleeding).

In instances of great loss of blood, such as in traumatic amputations, or extensive wounds, when surgical interference is necessary and would entail a certain amount of danger, should it be carried out, transfusion of a fairly large quantity of blood prior to the operation is of great benefit to the patient.

A secondary hemorrhage is also benefitted by blood replacement. Not only must one replace a large volume of lost blood, but the transfusion of fresh blood increases the coagulability of the patient's blood, which is of assistance in arresting hemorrhage. In patients suffering with hemophilia remarkable results have been obtained from the transfusion of a small quantity of blood. One instance of a child bleeding profusely from the tongue is cited. A small amount of the mother's blood was given intravenously, and within two hours a hard blood clot about the size of a cherry, formed at the site of the injury to the tongue. This dropped off after two days without any further bleeding.

In gall-bladder conditions in which there is obstruction with jaundice, general oozing of blood often takes place at the site of operation, with formation of large hematomata. In these patients, it is very difficult to control bleeding. The loss of coagulability of the blood is nearly always remedied by transfusion of whole blood. An instance of this kind in the author's experience is cited.

Hemorrhage from the stomach in ulceration following operation is often arrested by transfusion, and depleted circulation restored by a fair quantity of blood being transfused. With the citrate method one nearly always gets a reaction consisting of rise in temperature, chills and general discomfort of the patient, which, however, subsides in a couple of days. Reactions of this kind, but of a much milder nature, have occasionally taken place with the whole blood method.

Levine has observed hemoglobinuria following transfusion in two instances. Each of these patients died.

The quantity of blood to be given by transfusion depends on the condition that is being treated. When a patient has sustained no great loss of blood, and when the condition is one of toxemia, a small quantity is required in the transfusion.

In conditions of hemorrhage the average quantity of blood given is about 600 c.c., but the author has given as high as 1100 c.c. without any detrimental result.

The matter of selecting a donor is a very important matter for the success of transfusion. No blood should



be given to a patient without a hemolytic or an agglutination test having been done. The agglutination test is the simpler, easier and quicker method. Its technique is outlined as follows:

Have four small test tubes, two of which are to be used for red cells and two for serum. Mark one of the tubes to be used for red cells D R C (donor's red cells) and the other R R C (recipient's red cells). Into these drop 1 c.c. of sodium citrate of strength about 2 per cent. Allow two drops of donor's blood to drop into tube marked D. R. C. and the same quantity of recipient's blood into tube marked R. R. C. Into the other two tubes allow about 4 or 5 c.c. of blood to flow from donor and recipient for the purpose of obtaining serum. Wash the red cells with saline solution three or four times so as to get rid of the sodium citrate. The simplest way to wash these cells is as follows:

Add about 5 c.c. of normal saline to the tube containing the red cells, shake gently until thoroughly mixed, then put it in the centrifugal machine until red cells are deposited at the bottom of the tube and the fluid is clear above. Decant the clear fluid. Repeat this four or five times until the cells are thoroughly washed.

Take the two tubes containing the blood for serum and put them into the centrifugal machine so as to free the serum from the clot.

Take two glass slides and make a ring with vaseline at each end of the slide. These rings should be about the size of a five cent piece. Mark one end of the slide "D" (for donor) and the other end "R" (for recipient). Add a few drops of saline to the tubes containing the red cells so as to make a homogenous mixture. With a sterile pipette take one drop of the red cells mixture from the tube marked "D. R. C." and drop it into the circle marked "D" on the glass slide. With another pipette take one drop of the red cells mixture from the tube marked "R. R. C." and drop it into the circle "R" on the glass slide. To the drop of red cells in Circle "D" on the glass slide add one drop of recipient's serum. To the drop of red cells in Circle "R" on the glass slide add one drop of donor's serum. Mix well with a small glass rod. Add a cover-slip and put

in the incubator at 37° C. for one hour. In thirty minutes, if any agglutination is to take place, it will be shown under the microscope by the cells coming together in clumps, as is usually seen in a Widal reaction for typhoid. Examine again when the hour is up, so as to make sure of the condition. If no clumping has taken place, the blood is fit for transfusion.

The other test, namely, "the hemolytic test," is much longer as no reading can be done until after twelve hours in the incubator, and unless the case is a non-urgent one, this method is not to be made use of.

It has been demonstrated that no hemolysis will take place without an accompanying agglutination; but slight agglutination may take place without hemolysis. This, however, is not detrimental to the recipient, providing the reaction is not too great.

In conclusion, the author states that the medical profession now accepts the fact that great benefit may be derived from transfusion, if it is properly carried out. Excellent results obtained in numerous cases at the front have greatly strengthened the faith in transfusion as a remedial measure.

When modern methods are used, and ordinary surgical asepsis carried out, there need be very little fear of injurious results. Even if it should happen that transfusion is of no lasting benefit to the patient, it can certainly do no harm and is worth trying.

#### **The Intravenous Injection of Antimony in Filariasis.**

A preliminary report on the intravenous injection of antimony in filariasis is made by Sir Leonard Rogers.<sup>4</sup>

Owing to the difficulty in India, where this work was carried out, of following up native hospital patients, especially when they suffer so little inconvenience as in most cases of filaria in the blood, the author was not able to obtain conclusive evidence of the permanent value of intravenous injections of soluble antimony salts.

A study of thirteen cases constitutes the basis for this article. These thirteen were selected from a group of 105 with possible symptoms of filariasis, such as elephantiasis, lymphangitis, hydrocele or periodical fever, or abscesses.

(4) Lancet, Oct. 4, 1919.

One patient was kept as a control and twelve were treated, but two of the twelve are excluded from the final consideration on account of having received only four injections. The remaining ten received from five to eleven injections. In two cases 1 in 500 colloidal antimony sulphide was used in preference to tartar emetic, as the author has shown it to be less toxic.

In the case of both preparations the first dose was usually 2.5 to 3 c.c. and increased by 0.5 c.c. at each injection until the maximum of 5 c.c. was reached. The injections were made daily for eight days, and then every other day. It was the intention to continue the injections up to a total of twenty-four in some of the cases, but because of inability to control patients, this was accomplished in none of the cases. Not more than twelve injections were given to any one patient.

Apart from occasional coughing and slight nausea, and in one instance sickness, no toxic symptoms were observed.

The number of these parasites that circulate in the blood can be determined by using an ordinary blood-counting outfit, and staining the organisms with a diluting fluid of methylin blue. Therefore, the results obtained by this treatment were judged by the number of parasites before treatment and after treatment, as found by this counting method. All that is claimed for the work is that repeated intravenous injections of safe doses of sodium antimonium citrate appear to produce a definite diminution of the number of filarial embryos in the peripheral blood, which is probably due to a direct toxic effect on the embryos in view of the great decrease in the activity of their movements as observed just prior to a rapid diminution of their numbers.

Whether the treatment has any effect on the adult worms in the lymphatics or on the symptoms of the disease remains undecided, but the data so far obtained are sufficiently encouraging to make it advisable to continue their observation.

**Recovery of Flexner-Y Bacillus from the Blood During Life.** The recovery of the Flexner Y bacillus from the blood stream of a patient with bacillary dysentery

during life is reported by J. S. K. Boyd.<sup>5</sup> He says that it is a general experience that dysentery bacilli have been rarely recovered from the blood during life. Glynn, and his collaborators collected from the literature fifteen cases in which this had been accomplished.

The patient studied by Boyd was a corporal in the army, who came to the hospital complaining that four days previously he had become ill, with vomiting and diarrhea.

He developed an acute attack of bacillary dysentery, and the Flexner Y type of organism was isolated from the stools and from the blood. The patient recovered sufficiently to return to his duties and was not followed after that.

## ANEMIA

**Diagnosis and Prognosis in Pernicious Anemia.** Determinations of urobilin and urobilinogen in the stool of patients with pernicious anemia, with the object of knowing their value in diagnosis and prognosis in this condition has been made by G. H. Hansmann and C. P. Howard,<sup>6</sup> of Iowa City.

The material for this study consisted of twenty-seven patients, who had pernicious anemia, and as pathologic controls nine miscellaneous conditions, which included one case each of chlorosis, carcinoma ventriculi, purpura, familial hemolytic icterus, Banti's disease, lymphosarcoma, acute cholecystitis, hemochromatosis and tabes dorsalis.

The authors describe their method and tabulate and discuss the results.

The conclusions reached were as follows:

The evidence of abnormal hemolysis occurs first in the stools, secondly in the duodenal contents, and lastly in the urine.

An increase of the urobilin and urobilinogen in the urine and stools above 12,000 dilutions is a constant finding in pernicious anemia during the period of remission.

(5) Lancet, Sept. 13, 1919.

(6) Jour. Amer. Med. Ass'n, Oct. 25, 1919.

The presence of even small amounts of urobilinogen in the urine is evidence of a probable pernicious anemia in the absence of signs of biliary or hepatic disease.

A low red cell count with a low urobilin and urobilinogen count indicates an arrest of the activity of the disease process, and a period of improvement may be anticipated.

On the other hand, a high red cell count with a high urobilin-urobilinogen content indicates marked hemolysis and often precedes a steadily falling blood count, as has been demonstrated by Robertson and McCrudden.

**Duration of Remission in Pernicious Anemia.** The duration of remission in patients with pernicious anemia, is a most variable factor. What is considered to be an extremely long remission is reported by C. G. Stockton.<sup>8</sup> The patient was first seen by the author in 1899. The case was in all respects a typical one of pernicious anemia. There was irregular improvement for six years, at which time, although there was moderate anemia, the blood lost all characteristics of a pernicious type.

From 1907 to the beginning of 1918, the patient was considered to be well. Then there was a sharp recurrence which soon became threatening. The patient failed to respond to the action of atoxyl and sodium cacodylate, which drugs had formerly appeared to be of benefit.

A transfusion of 900 c.c. of blood from the vein of the patient's daughter led to temporary improvement. A week thereafter, the patient developed lobar pneumonia and died three days later, nearly twenty years from the recognition of her first attack of pernicious anemia.

This is thought to show that although a patient may escape all signs of the disease, save one, for a period of from ten to twelve years, yet the disease may recur. It is emphasized that there was a disappearance of all evidence of the disease save one, that one was the continuance of *achylia gastrica*.

In a long series of cases, private and hospital, studied during thirty years, the author has not found an exception to the rule of the presence, sooner or later, of *achylia gastrica*. Among the cases seen by him there

(8) Amer. Jour. Med. Sci., October, 1919.



have been several long remissions, but never has the gastric function been restored.

This persistence of achylia gastrica may have more significance than has been recorded, or accorded to it of late years. If it is granted that pernicious anemia is the expression of an infection, it is not improbable that gastric infection is in some way a link in the chain.

The belief prevails that an exceptional case of pernicious anemia goes on to recovery. It is questioned whether any one has ever reported the restoration of normal gastric secretion. In view of the fact that in this case, so far as is known, the most promising on record, the disease returned twenty years after its inception, and after having a remission in which there was to all appearances good health for a period of twelve years, the author feels that it may be concluded that a patient probably never entirely recovers from pernicious anemia.

The persistence of the gastric lesion points to a close pathologic relation between the stomach and the anemia. In this connection, attention is called to the observations of Seyderhelm of Strassburg, working with larvae of the fly *Estrus equi*, occurring in the gastric mucosa of horses suffering from a severe anemia, in its characteristics said to be suggestive of pernicious anemia in man.

**Studies of the Chemistry of Pernicious Anemia.** The work upon which this report is based consists of a chemical study of the blood and excreta from three adults who suffered with pernicious anemia. Besides presenting their own results, M. Kahn and J. Barsky<sup>9</sup> here give a brief *résumé* of the literature on the subject. Their study of blood from these patients showed a less specific gravity of the serum, a reduction of the protein content, an increase in the ash and lime content, and a normal fat cholesterol and glucose percentage. There was found a complete anacidity in the stomach, increased residuum and absence of pepsin resembling the gastric picture present in cases of carcinoma ventriculi.

The gastro-albumorrhea test was applied to the stomach contents of two patients. The total nitrogen in

(9) Archiv. Int. Med., March, 1919.

100 c.c. of gastric content was 4.1 mg. in one instance and 3.7 mg. in another. No albumin was present as determined by the phosphotungstic acid precipitation method. The authors say that it is to be assumed that there is no discharge of protein from the gastric mucosa, although there is, no doubt, a chronic inflammatory process in quantities sufficient to be tested.

The intestinal digestion was found disturbed. The fecal bulk was much increased, and the nitrogen loss in the feces was above normal. The fat in the feces was found to be normal. Intestinal putrefaction as evidenced by increased ethereal sulphate output was present. There was a state of suboxidation; the neutral sulphur-fraction was increased.

That the pancreas functionated normally was evidenced by enzyme examination of duodenal content, and feces.

A deficiency in the hepatic detoxication functions was shown by the sulpho-conjugation test. The glyco-genic and ureogenic functions of the liver were found to be normal.

It has been found by other workers that in pernicious anemia there is an excessive excretion of bile pigments or pleochromia and urobilinocholia. Pleochromia is an expression of immediate hemolysis, and which, in pernicious anemia, whether in crisis or remission, is a constant finding. Urobilinocholia indicates a heaping up of pigment in the portal system and varies directly as the portal system is surcharged or becomes relatively empty of the excess of pigment. It has been pointed out by Schneider that in secondary anemia neither pleochromia nor urobilinocholia is present.

The present authors found indication of excessive hemolysis in the patients studied as indicated by both a pleochromia and urobilinonochochia. In this regard they merely corroborate the experiments of Schneider.

A study of the chemistry of the urine revealed an increased elimination of oxyproteic acid nitrogen in these patients. The other urinary nitrogen fractions were normal.

Renal function as determined by the phenolsulphonephthalein test and the blood nitrogen partition was

found to be normal. The creatinin in the blood was increased. Acidosis was found in these patients as determined by the carbon-dioxide combining power of the blood plasma, the hydrogen ion concentration of the blood and the carbon dioxide of the alveolar air.

**Basal Metabolism Following Transfusion in Pernicious Anemia.** A study of metabolism in patients with pernicious anemia, who had received blood transfusion, has been made by E. H. Tompkins, H. H. Brittingham and C. K. Drinker,<sup>1</sup> of Boston.

After a brief review of the literature dealing with this subject, they state that on the whole experimental data have given evidence of a tendency toward increased metabolism in anemias of all types. Many explanations for this increase have been given, and they fall into two groups in relation to the experimental solution of the problem.

The increased muscular work required by the more rapid respiration and heart rate have been considered in most cases sufficient to cause such increase in metabolism as have been observed, with the exception of leukemia. This explanation depends on simple muscular compensation and demands no consideration of obscure toxic factors, metabolism of young red cells, etc.

The increased metabolism of young and nucleated red cells, unusual numbers of white cells, undetermined toxic influences and activity of the blood-forming centers have, with other possibilities, been cited as causes of the increased metabolism. None of these causes is definitely compensatory.

If the grade of the metabolism in anemia is due in any degree to the increased muscular work which the disease requires, it should be possible by reducing the heart rate and respiration to normal to gain a true picture of the uncompensated normal metabolism in the case. Blood transfusion, by an almost instantaneous check to the accelerated heart and lung action in these patients, restrains the muscular compensation. The authors have been unable to find record of work on the gaseous exchange under these conditions, and as transfusion was being employed by them in the treatment of

(1) *Archiv. Int. Med.*, April, 1919.

anemia, an exceptional opportunity for metabolic study was offered.

In the study of patients used in this work the authors gave transfusion of washed red cells, and thereby provided the simplest possible conditions—an increase in circulating hemoglobin without the introduction of material which can be burned, as is inevitable in the introduction of plasma.

The conclusions drawn from these results are:

Transfusion in these cases produced the following results: A diminution of metabolism; a diminution of pulse and respiratory activity; a drop in temperature if it had previously been elevated; a rise in percentage hemoglobin and in the simple blood count.

The response of the metabolism to transfusion lags behind that of all the other factors by an interval of several days. The lowering of metabolism is, therefore, not due simply to a cessation of the compensatory muscular activity of the anemic individual.

Before treatment the metabolism may be within normal limits or it may be above or below normal.

After transfusion the metabolism always reaches a normal or diminished level.

These facts suggest that the metabolism of the anemic individual is dependent on two contending factors, outside of any effects from compensatory muscular activity.

1. In untreated acute cases there is evidently some type of stimulation to the body cells in general and the amount of this stimulation is represented by the fall in metabolism after transfusion.

2. There are coincident progressive tissue alterations which tend to reduce metabolism. These alterations are represented by the diminished metabolism of the chronic cases, and by the low level to which the metabolism falls in practically all cases as a result of transfusion.

## DISEASES OF THE SPLEEN

**Etiology of Banti's Disease.** When Banti first described a condition that is now known as "Banti's Disease," or splenic anemia, he divided the disease into

three stages. In the first, anemia and splenic enlargement are found, the former being secondary to the latter; in the second stage, cirrhosis of the liver commences; and in the third, ascites sets in.

Later, the same author described more fully that form that is characterized by enlargement of the spleen, with cirrhosis of the liver and to this stage of the disease subsequent writers have attached his name.

This condition is manifestly only a late stage of the primary splenic enlargement, which in all cases precedes the anemia. The etiology of this disease is discussed in the present article by H. T. Kristjanson,<sup>2</sup> who states that the course of the disease and the fibrosis of the organs seem to suggest a chronic intoxication, possibly originating in the spleen. This theory is apparently supported by the great improvement, if not actual cure, in some instances, after removal of the spleen.

The author considers that the primary enlargement of the spleen, the anemia and cirrhosis of the liver, are all due to a common cause, a form of intoxication or infection. An opportunity for the etiologic study of the disease presented itself in a case admitted to the Milwaukee County Hospital, where the blood was studied before and after splenectomy. The histologic study of this spleen confirmed the clinical diagnosis of an early stage of splenic anemia or Banti's disease.

From cultures removed from the spleen of this patient, there was obtained an organism apparently closely related to, if not identical with the diphtheroid bacillus constantly found in frank cases of Hodgkin's disease.

These organisms were used in an attempt to reproduce the disease in animals. The effects produced on dogs by repeated intravenous inoculations with the organism were marked systemic reactions indicated by rise in temperature and leukocytosis. These experimental inoculations in the dogs produced progressive enlargement of the spleen, with gradually increased fibrosis and perisplenitis. The histologic changes in spleens were quite like those in early Banti's disease. Control animals inoculated under identical conditions with staphy-



loci, colon bacilli and pseudo-diphtheria bacilli, showed no progressive fibrosis of the spleen but had symptoms of general infections to which they succumbed. The change in the blood picture of these control animals was that of leukocytosis, while in the other experimental animals the change was that of a type of secondary anemia.

As a constant feature, the experimental animals inoculated with the organisms isolated from the spleen in Banti's disease gave a positive complement-fixation, using a bacterial antigen and the sheep's hemolytic system.

Thus there were produced by experimental inoculation of animals with the organism obtained in Banti's disease, changes in the spleen which were identical histologically with the spleen from Banti's disease. Other organisms similarly injected did not produce these changes.

**Gaucher's Disease in Adults.** A study of the histopathology, biology and chemical findings in Gaucher's disease, with a record of two patients who presented this condition, is published by F. S. Mandlebaum,<sup>3</sup> of the Mount Sinai Hospital, New York.

Clinically Gaucher's disease is said to begin in infancy or childhood, and is characterized by a progressive enlargement of the spleen, and subsequently of the liver, a discoloration of the skin of the exposed parts of the body, a peculiar thickening of the conjunctivae, a tendency to hemorrhages, such as epistaxis or bleeding from the gums, and a definite leukopenia.

The superficial lymph nodes are not enlarged, jaundice does not occur and ascites is rare. The disease is distinctly chronic and terminates as the result of a complicating affection. The organs involved are the spleen, liver, lymph nodes and bone marrow, the distinctive feature being the presence in each of these organs of large cells showing a peculiar type of cytoplasm not exactly duplicated in any other pathologic condition.

The first patient reported by the author was a married woman, 41 years old, who complained of pain in the left hypochondrium and precordial region, cough, night-sweats, fever of four weeks' duration and blood-tinged

(3) Amer. Jour. Med. Sci., March, 1919.

sputum for one day. She had lost more than twenty pounds in weight in the course of ten years. By physical examination there were found systolic heart murmurs, and an enormously enlarged and movable spleen reaching into the pelvis. The liver extended from the fifth intercostal space obliquely downward into the right iliac fossa. A pale brownish discoloration of the skin of the face was noted, especially on the forehead. The superficial lymph nodes were not appreciably enlarged. No thickening of the conjunctiva was seen. The hemoglobin was 54 per cent., red cells, 2,720,000; leukocytes, 2600. In a differential count of 100 leukocytes, 4 normoblasts were observed.

Splenectomy was performed upon this patient and immediately after the operation a transfusion of 400 c.c. of blood was made. Following this the blood picture was practically unchanged, while the patient remained in the hospital and a moderate leukocytosis of from 7000 to 21,000 persisted, with a fairly normal ratio of lymphocytes to polymorphonuclears. The patient gained thirteen pounds in weight and was discharged, about two months after the operation.

The spleen weighed 4250 grams, or 9 pounds and 6 ounces, and measured 38 cm. on the long axis, 16 cm. in width at the upper pole, 21 cm. at the lower pole, with an average thickness of 9 cm.

In frozen sections of the fresh spleen no trace of fat or lipoid and no anisotropic bodies could be found. Histologic examination of sections preserved in Zenker's fluid revealed that the pulp was almost entirely replaced by large round, or oval alveolar spaces containing the characteristic cells found here in this disease. A small amount of bright yellow pigment was found in the sections. This was in the form of minute crystals lying free or contained in small reticular cells. The pigment gave a positive reaction for iron. There was no positive evidence in these sections that the Gaucher cells are phagocytic for erythrocytes.

That lipoid substances could not be found in the Gaucher cells was further confirmed by microchemical methods.

The second patient was a man, 37 years old, who had

had a growth in the abdomen for a period of twelve years. He complained of sharp pains in the left hypochondrium, radiating to the shoulder, and extending over the entire abdomen. No history of fever or loss of weight was given.

On physical examination the spleen was found to be greatly enlarged. The liver was not apparently enlarged and could not be palpated. There was distinct evidence of fluid in the abdomen. Many brownish colored patches and scars were seen on the legs. Secondary anemia was very evident. The Wassermann reaction was negative. A diagnosis of Gaucher's disease was made on this patient, and splenectomy was performed soon afterward. Many dense adhesions were found over the spleen, which prolonged the time of operation. A blood transfusion of 600 c.c. was performed immediately after the operation, and eighteen days later the patient died.

The spleen weighed 3500 grams, or 7 pounds, 11 ounces, and measured 25 x 18 x 12.5 cm. Smears made from a freshly cut surface of the spleen showed many characteristic large cells with multiple nuclei. Frozen sections were made and no lipoid substances or fat could be found. Polariscopic examination for double refracting substances was also negative. The histologic picture was almost identical with the one mentioned above.

At autopsy, the liver was found not to be enlarged, contrary to the rule in cases of Gaucher's disease, but the picture in it was typical. There was an enormous increase of interstitial connective tissue. Large masses of Gaucher cells were seen in the meshes of interstitial tissue and also invading the peripheral portion of the lobules.

The degree of involvement of lymph nodes varied in the different regional groups. Those in which the process was far advanced showed an almost complete disappearance of normal lymph-adenoid structure, the entire node being replaced by the characteristic large cells.

In the bone marrow, the large cells were seen single and in extensive groups and presented the general characteristics noted in the other hemopoietic organs. No pigment was seen.

Other careful microscopic examination was made of the heart, aorta, lungs, thymus, kidneys, adrenals, pancreas and intestines. No large cells could be found in any of these organs, corroborating the findings in all previous authentic cases.

Concerning the presence of large cells in other conditions, the author states that numerous investigators have shown that certain groups of cells, notably the reticular cells of the hemopoietic organs are susceptible to the effect of various agents. Mallory described certain cellular changes in the spleen, lymph nodes, bone marrow and liver in cases of typhoid fever. These were designated as endothelial leukocytes, and the biologic importance of these cells reacting as a group to a definite toxin was recognized.

The tubercle bacillus is another agent capable of producing cellular reactions in this group of cells, especially in the spleen and lymph nodes.

The injection of carmine or acid colloidal dyes into animals produces changes in the same specific group of cells as affected in Gaucher's disease. The cells thus produced have been given the different names by the various authors who have worked on the subject.

Concerning the large cells found in certain organs of patients who have Gaucher's disease, the author after a careful study of the tissues from the two patients mentioned above, says, that in the nodes in which the involvement is far advanced the follicles or remnants of follicles are always surrounded by a ring or wall of large cells and in the center of the follicles large cells are seen. The process begins in a small group of large cells in the germinal center or at the periphery of the follicle. These cells spread until the follicle is almost surrounded, and the cells also spread outward from the germinal center. In this way the follicle is gradually replaced by Gaucher cells and the lymphocytes gradually disappear. The significant fact, is that the Gaucher tissue occurs in those regions in which the reticulum shows distinct evidence of hypertrophy. The cellular reticulum in normal lymph nodes is very abundant in the germinal centers and a thick layer may surround the follicle. In both regions it changes its character very

readily whenever the node is placed under abnormal conditions of any kind. Downey has shown by tracing strands of normal reticulum that they finally loosen up and assume the same identical structure as the Gaucher cells, proving beyond question that the Gaucher cell is merely modified cellular reticulum—that is, modified by the storage of some foreign substance taken up. This accounts for the apparent fusion of Gaucher cells into syncytial masses and for the long cells, and also for a reduction in the amount of normal reticulum within the masses of Gaucher cells.

The so-called endothelium which lines the sinuses is absolutely normal. The present view is that this "endothelium" is really a part of the general reticulum. The Gaucher cells therefore are considered as certainly not of "endothelial" origin, and the material presented here shows no evidence for the transformation of the reticulum bordering any of the sinuses of the lymph nodes into Gaucher tissue. The reticulum lining the sinusoids (Kupffer cells) is not involved in the process, therefore, the origin of the free Gaucher cells within the sinusoids must be accounted for in some other way. That these cells are carried into the liver through the splenic vein seems probable, as the Gaucher cells are frequently seen in the larger branches of the portal vein.

From what has been described in the lymph nodes, it is evident that the histogenesis of the large cells in the spleen is the same, but the process in the spleen in all the cases examined by the author is too far advanced to permit of the same accurate determination as in the lymph nodes.

From the foregoing description it may be seen that a definite and characteristic reaction of the reticulum of the hemopoietic system occurs in Gaucher's disease.

The subject of lipid substances in the large cells of Gaucher's disease has been investigated in six cases, four children and two adults. In two of the cases it was possible to use only material fixed in formalin, but in the remaining cases, two children and two adults, fresh material was also employed. From this part of the study Mandelbaum concludes that the peculiar substance in the cells which is so characteristic of Gaucher's dis-



ease, and which has never reacted to any microchemical method for lipoids is not of pure lipoid nature. The substance does not lie in the extractive group, but is, in all probability, of complex protein nature in combination with lipoids.

In conclusion, he says that other diseases, as well as some lesions produced experimentally in animals, may be accompanied by the presence of large cells involving the same specific group of cells that are concerned in Gaucher's disease. This group, as has been shown, may react in various ways to many forms of irritation, chemical, bacterial, metabolic or toxic in character, but the changes in each instance are dependent upon variable etiologic factors, and a clear distinction between these cellular reactions and the large cells of Gaucher's disease may be made microchemically and histologically.

## DISEASES OF THE DUCTLESS GLANDS.

### THE THYROID.

**A Method of Testing Thyroid Function.** A detailed description of clinical results obtained with a method of testing thyroid function is presented by Henry R. Harrower.<sup>1</sup>

Based upon a number of clinical experiences of producing excessive irritableness, hyperexcitability and heart disturbances in patients by giving them thyroid, the author has devised a very simple but none the less useful method of testing the thyroid function. This consists of giving definite and increased doses of thyroid extract, with a suitable inert excipient, in a uniform and routine manner, while a careful and regular study is made of the pulse and other symptoms which may ensue. The information obtainable in this manner is of much service, for it amounts virtually to a differential diagnostic measure in the study of goiter.

It will be recalled from the secretory standpoint that there are two distinct varieties of goiter: (1) the simple enlargement of the gland which appears to be an effort on the part of the organism either to supply an increased demand for its particular product which may be deficient, or to produce a greater supply than usual because of an increased demand for it; and (2) the hypertrophy, which is due to some extraglandular cause, such as toxemia or any form of irritation. The former, or simple goiters, are a useful attempt on the part of the body to render the best service possible under the circumstances and these patients are usually benefitted by a course of treatment which includes the administration of thyroid, iodine, etc., which thus tends to supply the need, in part at least, and render the friendly aid of the gland unnecessary.

In cases in the other class, however, the conditions are decidedly different, for the thyroid gland is being over-

(1) Med. Record, Nov. 1, 1919.

worked and driven faster than normal. This condition is usually brought about by the toxins absorbed from foci of infection, from emotional disturbances or from deranged functions of some of the other endocrine glands. In such cases, the thyroid gland is more sensitive and hence more unruly; and just as the hypertrophy differs very materially in origin, so it differs in its responsiveness to treatment. In fact, what would be most beneficial in simple goiter would be most detrimental in the goiter due to hyperthyroidism, and the administration of this "thyroid function test" enables one to differentiate the early functional stages of thyroid sensitiveness, *i. e.*, between latent hypothyroidism and hyperthyroidism, and accomplish something worth while in the treatment.

The materials for the thyroid function test consists of four doses each of  $\frac{1}{2}$ , 1 and 2 grains of thyroid in graduated capsules together with a chart, to which is attached printed instructions for taking the capsules, four  $\frac{1}{2}$  grain doses the first day, four 1 grain doses the second day, and four 2 grain doses the third day. The pulse is recorded five times a day, and charted as directed in the instructions.

In the apathetic hypothyroid cases, practically no difference in the pulse figure is found, and as in these cases cardiac action, like practically every function of the body, is lazy and slow, the pulse figures are low and remain so.

In the normal individual, thyroid feeding temporarily stimulates the thyroid function, and hence, through it, the heart-rate, and an increase in the pulse is customary, during the third day of taking the capsules.

The cardio-stimulant action merely lasts during the time of the greatest dosage of thyroid and comes down to normal again the day after.

On the other hand, in the various stages of thyroidism, the pulse findings are characteristic; the greater the susceptibility, the wider the range. It may reach well above any possible normal figure, 110, 120 or even higher. Since this stimulant is due to the increased activity of the supersensitive gland, following the removal of the medication, the pulse still remains up,

because the thyroid is working overtime. In well-defined hyperthyroidism, with tachycardia, this test should not be used. The test is more useful in the discovery of thyroid apathy, or a latent degree of thyroid sensitiveness than in the diagnosis of frank hyperthyroidism.

The chief advantage of the test, is that it presents a definite scheme for determining the sensitiveness of the thyroid to stimulation, and recording the results in such a way as to render them of distinct value to the physician.

**Goiters in Young Men.** This discussion of goiters deals largely with the endemicity of the condition. The author, Simon Levine,<sup>2</sup> observed abnormalities of the thyroid in registrants of Division No. 2 of Houghton County, Michigan, while serving on the examining board at that place. On examination of 583 registrants, he found that 177 of the men, or 30 per cent., showed a demonstrable enlargement of the thyroid; of the total number examined, 140, or 24 per cent., had simple goiters. Twenty-three, or 3.9 per cent., had toxic goiters, and fourteen, or 2.4 per cent., had large goiters of the adenomatous colloid or cystic type of a disqualifying nature.

By an investigation of the places of birth, it was found that of 155 men of 21 years of age, all but three were born in a section of the goiter belt. Therefore, the presence of goiter in 95 per cent. of the cases of young men marked the place of birth. The decreasing percentage as the registrants grew older was evident and was considered to be due to the fact that a certain proportion of older members of the community may have been born elsewhere and that they had traveled in non-goiterous districts.

Of the total number of disqualifying defects, goiter furnished 20.9 per cent., or more than one-fifth. It is the author's opinion that 30.3 per cent. is a true proportion of goiters in males in this district. The figures show that in registration division No. 2, of Houghton County, Michigan, there were 9,615 goiters 1,999 of which were of a disqualifying character. The word "disqualify-

<sup>22</sup> Jour. Mich. State Med. Soc., March, 1919.

ing" is used to mean large, toxic goiters according to the definition in the selective service regulations. It is estimated that in Houghton County there are 26,694 goiters, of which 5,550 were of the disqualifying type, and in the Upper Peninsula of Michigan 98,665 goiters with large and toxic types numbering 20,515. The economic and social importance of these figures cannot be denied.

**Studies of the Thyroid Gland Among Soldiers at Camp Lewis.** A survey of 21,182 troops at Camp Lewis, Washington, from eleven states, comprising an area of approximately one-third of the United States, was made by W. J. Kerr.<sup>3</sup> There was found a high incidence of simple goiter in certain regions. The incidence was highest in Washington and Oregon, and lowest in California and Nevada. There is an area of endemic goiter largely confined to the Pacific Northwest, and shading off to the south and east. There is again a slight increase in Minnesota which should be considered as a part of the endemic goiter region adjacent to the Great Lakes.

Exophthalmic goiter was rarely seen in troops coming to this camp, although many recruits were rejected because of thyroid enlargement producing pressure symptoms or interfering with the wearing of the military collar. Cases of exophthalmic goiter were rejected by the local boards.

Twenty-one per cent. of all troops examined showed a definite enlargement of the thyroid gland. Of these, 27 per cent. showed a large or moderately enlarged thyroid, and 73 per cent. were classified as "small." In the latter group only those in whom the gland could be distinctly felt on swallowing were included.

The enlargement of the thyroid gland was noted as diffuse in 38 per cent. of the cases, isthmus in 52 per cent. right lobe in 5 per cent. and left lobe in 4 per cent.

The family history of the recruit with enlarged thyroid glands showed that goiters had been noted in sisters three times more frequently than in brothers, and in mothers ten times more frequently than in fathers.

There was no evidence to show that the thyroid gland

---

(3) *Archiv. Int. Med.*, September, 1919.



disturbance diminishes in frequency between the ages of 21 and 31 years.

Such physical signs as tremor, tachycardia, vasomotor instability of the hands and curved nails, were noted, and were found in a larger percentage of men with thyroid enlargement than in those without demonstrable changes in the gland. The differences, however, were not striking and no definite conclusion can be drawn at this time.

No definite conclusion can be drawn as to the etiologic factors in the production of endemic goiter. The region affected roughly corresponds to the glaciated areas of the United States. There is apparently some relation to the water supply.

**Hyperthyroidism in Recruits.** This discussion of hyperthyroidism by Sidney Kuh<sup>1</sup> is presented as a result of his experiences on a medical advisory board during the recent war. Large numbers of cases of hyperthyroidism with just a few symptoms of the malady, as tachycardia, goiter, tremor of the hands and infrequent blinking were encountered in examining men for the army. Comparatively few of the men were conscious of any illness. The experience was similar to that encountered in private practice.

Of the misleading complications associated with this disease, Kuh says that probably the most frequent and important ones are to be found in disturbances in the gastro-intestinal tract. Other complications seen which obscured the picture of exophthalmic goiter, because they were responsible for the only symptoms of which the patient complained, were muscular atrophy; an hysterical pseudo-chorea; an agoraphobia; the morbid fear of picking up a pocket book belonging to somebody else and thereby laying one's self open to the suspicion of being a thief; the fear of becoming insane; a typical picture of Addison's disease in one instance, and in another a marked brownish pigmentation of the lower lids; mucous colitis; in several instances the symptoms of dementia praecox; attacks of *petit mal*; chronic spasm of the sternocleidomastoid muscle, probably hysterical; manic-depressive insanity, this last-named instance occurring

(4) Illinois Med. Jour., April, 1919

in a patient sent by a neurologist who had overlooked the symptoms of hyperthyroidism. These experiences are listed from the author's private practice. In two instances his patients complained of marked somnolence, in place of the insomnia so commonly found.

In answer to the question: "what is the cause of hyperthyroidism?" he states that in many instances the first symptoms appeared at about the age of puberty, and emphasizes the fact that in taking the history of the person suffering from this disease, careful questioning should be made in order to determine whether or not there were signs of goiter from the age of puberty to 20 years of age.

In reciting the most common symptoms of Graves's disease, tachycardia is mentioned first. While this symptom is commonly indicated by a pulse rate that is only very moderately increased when the patient is at rest, it will become markedly increased on slight exertion, and even more so with every trifling excitement. Other important early symptoms are attacks of diarrhea independent of any error in diet; falling of hair; a feeling of distress in the gastric region after meals and, at times, headaches followed by nausea, chills, vomiting, dyspnea and violent palpitation. Very striking and characteristic is a peculiar change in the complexion; a muddy hue being prominent in this respect. A slight rise in temperature is also a very constant symptom.

With the most careful history taking and examination there will remain instances in which suspicion is aroused, but in which a definite conclusion as to the cause of illness cannot be reached. If the patient in such a case is a woman, careful watch should be made to see whether or not there is an exacerbation of the symptoms during the menstrual period. This will frequently assist in making the diagnosis. Hyperthyroidism is to be looked on, therefore, as a common disease. It is found as a complication in innumerable cases of the so-called functional neuroses, and very often overlooked because of the tendency to waste little time in the examination of a "neuro."

In discussing the treatment of this disease, the author refers to his results in the use of serum from thyroidecto-

mized animals. His experience is based upon observations of hundreds of cases which he has treated in this manner. He gives from 50 to 60 drops of the serum by mouth three times a day, and considers this by far the best remedy that can be used for the disease. While accurate figures are not presented dealing with the patients treated, because of the fact that they have been treated in many different dispensaries, he says that 90 per cent. of the cases of hyperthyroidism thus treated have reacted favorably to the serum. It is only when this treatment has failed that one should send the patient to a surgeon.

**Symptoms of Hyperthyroidism in Exhausted Soldiers.** In the latter part of 1917 Major W. Johnson,<sup>5</sup> R. A. M. C., was able to observe and take brief notes on fifty soldiers who suffered from exhaustion and presented symptoms of hyperthyroidism. These men were admitted into a center for psychoneuroses and formed a small percentage of the total admission for this purpose.

Concerning the relations between emotions and the internal secretions, Johnson points out that the observations of Cannon have made it clear that there is an increased output of adrenin into the blood-stream produced by profound sympathetic activity, and the physical manifestations of emotions are the result of this increased output of adrenin. He notes, further, that an increased adrenin secretion causes an increase in the blood sugar, an improvement in the contraction of a fatigued muscle, an increase of the coagulability of the blood, a rise in the blood-pressure by constriction of the splanchnic area, and an increase in force and frequency of the cardiac beat.

In view of the cases described in this article the author adds the generally accepted view of the function of the thyroid secretion which is as follows:

A re-enforcement of the action of adrenin; the production of mental inactivity, this is, myxedema and cretinism, when it is absent or diminished; and the production of a state of mental excitement when it is present in excess. In an individual who is exposed to emotional stress for weeks, sometimes months, without being

(5) Brit. Med. Jour., March 22, 1919.

able to perform the active bodily movements, fighting, running, etc., which are the natural expression of the emotions, the increased internal secretions which have been produced in the body, become, as it were a drug on the market. Their physiologic cycle is uncompleted, and when the emotional state has been excessive and prolonged, as was the case of soldiers under recent military conditions, it seems possible that the accumulation of the excessive products of internal secretions in the body may produce pathologic conditions.

It would appear, then, that the various symptoms exhibited by men breaking down in the line have a definite basis. The patient presents those states which are recognized as being produced by sympathetic activity, but presents them in a riotous way. He has palpitation and tachycardia, disordered activity of the alimentary canal, dilated pupils, protrusion of the eyeballs, sweating and vasomotor disturbance. Added to these are the various subjective complaints which are the results of these states, that is, headaches, dizziness, dyspepsia, indigestion, loss of weight, weakness on exertion and that general unhappy condition described as nervousness.

This group of fifty men formed one clinical group and varied only in the degree with which the symptoms were exhibited. The ages of the patients varied from 21 to 43, the majority being between the ages of 23 and 35.

In only one instance was a history obtained of a previous condition of exophthalmos. In general appearance the man who was typical in this group was pale, looked ill, had suffered from loss of weight, had a skin that was soft and moist, and extremities that were, as a rule, cold and cyanosed. The mental state was usually one of subdued excitement. The men were worried and had little or no emotional control.

A serious result of this state of mental tension was the excessive irritability presented; prominence of the eyes was observed to some degree in all cases. The facial expression was one of fear and anxiety. Von Graefe's sign and Joffre's sign were each present in those cases in which the exophthalmos was most profound. Muscular movements were carried out in a quick excitable manner, and any effort easily produced sweating and a

sense of fatigue. Tremor was a constant phenomena. The nervous reflexes showed slight alterations. The pupils were usually slightly dilated and gave a slow diminished reaction to light. The tendon reflexes were always exaggerated. The subjective symptoms varied widely. Complaints of being nervous and weak, of throbbing headaches, dizziness, palpitation and precordial pains, digestive discomforts and diarrhea, frequency of micturation and irregular sleep were prominent among the complaints. The whole general state of the individual was one of querulousness and anxiety—the attitude of the man who feels that he can not drive himself one step further.

It was found that after a rest in bed with full diet, suitable tonics, and occasionally Dover's powders at night, the condition of all patients rapidly improved in from ten to fourteen days.

The condition described in connection with "effort syndrome" was frequently found, the cardiac impulse being diffuse and heaving in character. The pulse rate varied in wide range, around from 80 to 130. Blood-pressure ranged from 126 mm. to 148 mm. of mercury, and did not appear to show any relation whatever to variations of the pulse-rate.

Pallor and sweating of the face associated with a cold, moist and dusky cyanotic condition of the hands was frequently observed. Samples of blood from six patients failed to show the presence of any hyperglycemia. In about one-third of the cases the urine was tested and no reduction of Fehling's solution occurred.

The adrenalin test was carried out by placing two drops of the ordinary adrenalin solution (1 in 1000) into the eye in a few cases. No positive local or systemic changes were observed. The effect of deep pressure on the eye balls upon the pulse-rate was not constant. In some instances the pulse was markedly slow, but in many others there was but little change.

From this study the author is led to believe that a large number of so-called psychoneuroses are cases in which the symptoms are due to a state of disordered internal secretions, the result largely of emotional exhaustion, and to a less degree of physical exhaustion;



that many cases which are later diagnosed as irritable heart, D. A. H., soldier's heart and neurasthenia, are really cases of this class, and that possibly many have passed through a slight state of exophthalmos without its importance being recognized. He suggests, therefore, the advisability of classing the whole group under a suitable term. "Exhaustion syndrome" would appear to be the most applicable, and would possess the great advantage of not suggesting a period of chronic invalidism, such as a soldier associates with D. A. H., neurasthenia and similar terms.

**Simple Goiter.** This question is discussed by M. H. V. Cameron,<sup>6</sup> of Toronto. Normal function of the thyroid is first considered. Reference is here made to the statement of Kendall who describes the function of the thyroid as elaboration of a catalyzer, the alpha-iodine compound, which regulates the rate of de-aminization of the amino-acids and as the regulator which gives to each cell the adequate supply of this catalyzer momentarily, the colloid functioning as the vehicle of reserve. He also suggests that the function of the parathyroids is to convert ammonium carbonate into urea and that therefore the urea-ammonia output is a measure of thyroid-parathyroid activity.

A clinical classification of goiters has been made by Crotti, who divides all goiters into benign tumors, malignant tumors and tumors of inflammatory origin. His classification is presented here:

The benign tumors are:

I. Parenchymatous goiter,

1. Physiologic (puberty, pregnancy, etc.).
2. Non-toxic.
3. Toxic.

II. Colloid (cysts, fibrous, calcareous and osseous).

III. Fetal adenomata.

The malignant tumors are:

1. Epithelial tumors with seven subclasses.
2. Connective tissue tumors, with six subclasses.
3. Mixed tumors, with five subclasses.
4. Dermoids.
5. Accessory thyroids.

<sup>66</sup> Canadian Med. Ass'n Jour., April, 1919.

## Inflammations:

## I. Bacterial:

1. Acute (non-purulent, purulent).
2. Chronic (syphilitic, tuberculous and woody thyroiditis).

## II. Toxic.

III. Parasitic—Chagas's *Chizotrypanum cruzi* and *echinococcus*.

The first type, or parenchymatous goiter, is characterized by an increase of all the glandular elements of the thyroid. There may be an increase in colloid. There is an increase in iodine content. In its simplest form it is "the hyperplasia for physiologic reasons" described by Edmunds. The increased demand for the secretion induced by the strain of puberty or pregnancy is met by this increase in glandular elements, and, lest it pass on to hypertrophy which characterizes the nontoxic form of parenchymatous goiter, it becomes necessary to spare the thyroid by feeding thyroid extract or by administering iodine in some form, preferably and ideally the new alpha-iodine compound of Kendall.

Colloid goiter is due to an excess production of colloid, which is described as a spongy material which aids in the storage of iodine, a vehicle of reserve. The excess production of this material under undue stimulation to hormone elaboration, when metabolism is speeded up for one cause or another, may, after the stimulus has been removed, leave a mass of colloid which is not absorbed and so be the beginning of a simple colloid goiter. This form of goiter is then characterized by a great increase of colloid material, and by a decrease in iodine content. It may develop into cystic, fibrous, vascular or calcareous goiter, forms whose names are self-explanatory.

Fetal adenomata are rests of the masses of undifferentiated cells which are intermediate between the cylindrical cells of the thyroglossus duct and the typical cells of the normal thyroid gland.

Malignant tumors of the thyroid are important, especially in that it is most necessary to differentiate them from benign goiters at a stage in which operation may give some hope of cure.

The inflammations of the thyroid are bacterial, toxic or parasitic. Their consequences may vary according as the process occurs in a normal gland or a goiter.

The clinical symptoms of simple goiter are systemic disturbances, such as a slight thickening of the skin, constipation, apathy, etc., or slight tachycardia, impatience, brilliance of the eyes, nightmare, nervousness; etc. In every goiter there must be a transition stage before the definite symptoms of a degeneration leading to hyperthyroidism or to the onset of a toxic condition.

The etiology of goiter is still an unsolved question. There is considerable evidence to show that heredity plays a part particularly in the production of cretins. Goiter in the mother has a greater influence than goiter in the father. It has been demonstrated that filthy living conditions tend to goiter formation. All these theories have their advocates, but the most generally accepted and best proven etiologic factor in the production of endemic goiter is water. The query is made as to what is in the water. The occurrences of so-called "goiter-belt" is generally accepted but variously explained. Many theories as to the content of water that may produce goiter have been offered. It is described as a colloid substance, removable from goiterigenous water by dialysis, killed by boiling, by treatment with zinc hydrate or hydrogen peroxide. It is described as a radioactive body derived from the plutonic origin of the waters concerned, and it is held to be an infection. How an infection has persisted from the paleozoic age until the present surely demands proof. Another theory is that a characteristic of goiterigenous water is a content of fluorides.

Other etiologic factors general to goiter, are circulatory disturbances, abnormal nervous stimulations, and absence of iodine in food.

[There is clinical and laboratory proof that the chronic inflammatory goiter is not infrequently due to foci of infection located in the head.—B.]

The treatment of goiter is prophylactic, medical and surgical. Prophylaxis may be obtained by avoiding residence in goiterous regions. Pregnant women who live in a goiterous neighborhood should have treatment with

thyroid extract. Nursing women who have goiter should have similar treatment. In goiterous areas, the best prophylactic measure is that of boiling the water for twenty minutes.

Under the heading of medical treatment, Cameron says that the hyperplasia of the thyroid seen at puberty may well respond to a general supporting treatment, that is, syrup of iodide of iron, a sojourn by the sea, and the use of iodine by placing an open bottle of the crystal material in a school room or in the bed room. The toxic forms all benefit greatly and many will be cured by prolonged rest in bed, and more or less complete isolation. To this might be added treatment by calcium iodide. Quinine hydrobromide may also be found useful.

Surgical treatment is the only one, he says, to be used in the treatment of malignant goiter, in advanced colloid and cystic goiters, and in the nodular form.

**Hyperthyroidism.** The present conception of hyperthyroidism is based on what is known of the physiology of the thyroid gland and its changes in disease. There are two known products of the glands: Colloid and its hormone, or the alpha-iodine compound of Kendall. The gland's function is the determination of the amount of energy any cell in the body can produce upon stimulation, either from within or without. An increase in the hormone will produce increased activity of the glands, increased energy of all cells and, therefore, increased metabolism.

For the purpose of studying metabolism in these patients, says J. K. McGregor,<sup>7</sup> a period of complete rest for fifteen minutes is first provided; then a mask is tightly fitted over the face, through which is inhaled outside air from which leads a tube carrying the exhaled air to a gasometer. The percentage of oxygen in the air is a known quantity, 21 per cent. The volume of air exhaled in a given time, and the percentage of carbon dioxide therein is estimated. The amount of carbon dioxide when compared to the oxygen taken into the lungs, will give the amount consumed within the body, or, in other words, the amount of fuel consumed in the production. This, when figured with the square body

(7) Canadian Med. Ass'n Jour., May, 1919.

surface (after Dubois table) is expressed in percentage of metabolism. The normal being zero, with an element of error of 5 per cent. either way, hyperthyroid cases usually run an average of plus 50 per cent. and may run as high as plus 140 per cent. The practical side of this test, so far as it has gone, is, that the group of cases showing symptoms of tachycardia from psychic or other causes will not show an increase in metabolism.

This process may also be used to differentiate adenomas of the thyroid from exophthalmic goiter and as an index as to whether enough gland has been removed at a surgical operation, whereas previous to this it has been pretty much a matter of conjecture.

The symptoms of exophthalmic goiter, given in the order in which they usually make their appearance, are as follows: Cerebral stimulation; vasomotor disturbances of the skin; tremor; mental irritability; tachycardia; loss of strength; cardiac insufficiency; exophthalmos; diarrhea; vomiting; mental depression; jaundice.

In regard to the course of the disease, it increases gradually to its greatest height during the first year and gradually falls with intermittent exacerbations during the next three or four years. The sex proportion is about three females to one male, and the disease is most common in the second, third and fourth decade.

In the differentiation between exophthalmic goiter and tachycardia due to other causes, where possible, the metabolism test should be used.

If surgical treatment is to be resorted to, the selection of time for surgical interference is of utmost importance. In McGregor's opinion, the mental state of the patient is by far the best index of the safety of surgical procedure.

The ligation of one or both thyroid arteries, or the injection of boiling water into the gland are recommended as excellent preliminary steps in the surgical treatment. The removal of the gland may be undertaken in from ten days to several months after this preliminary treatment, depending on the reaction.

A patient is considered cured only when all the symptoms have entirely disappeared. If this is accepted 75 per cent. of the cases will be cured or able to carry on



their ordinary life duties; 20 per cent. will be improved, and 5 per cent. will show very little if any change.

The author has had one death in fifty-three patients who have come to operation. In this case no preliminary operation was done.

### **The Course and Prognosis of Exophthalmic Goiter.**

This rather lengthy discussion of the course of exophthalmic goiter by Israel Bram<sup>8</sup> is interesting, contains many important points, and is based in a large degree on the author's own personal experience.

Concerning the outcome of the patient with exophthalmic goiter, he says that the individual may be considered cured when the active process of thyroid intoxication has been made to cease. It is well to remember, however, that no matter how mild a disease appears, there is always a certain amount of permanent damage of this or that part of the economy just as there is always a variable degree of scar tissue remaining after laceration of one of the tissues. So that a word "cure" even at its very best, is but a relative term and concerns more the patient's subjective feeling, his practical usefulness and relative longevity, rather than the complete pathologic or histologic restoration of each individual cell concerned in the morbid process.

In considering the mortality of Graves's disease it is to be remembered that fatal terminations are tabulated as direct and indirect, and that if these two are considered together the mortality of the disease is perhaps 18 or 20 per cent. In addition to the fatalities from Graves's disease itself, the indirect causes of death during the course of hyperthyroidism must be considered. First under this heading comes heart failure or loss of compensation due to the profound degeneration from over-activity of the myocardium. Also, tuberculosis frequently either co-exists at the onset of the Basedowian syndrome or asserts itself sometime during its course. Other items listed under this heading are insanity in some form, myxedema, which is superimposed on the hyperthyroidism, cachexia strumipriva, resulting from the removal of the entire thyroid gland, tetany, due to the removal of the parathyroid gland and, finally, in rare

(8) Archiv. Diagnosis, January, 1919.

instances, diabetes mellitus which either precedes or inter-curs, or which may follow some time after the onset of hyperthyroidism.

Concerning the factors that are capable of influencing the course and prognosis of the disease, Bram gives the following as the most important; they are divided into intrinsic and extrinsic:

In the former class the first items are age and sex. The younger the patient, the more severe the symptoms. The author's youngest patient was a girl 13 years old, and his oldest, a man, a physician, 64 years old. Next in importance is the previous condition of the health of the patient by virtue of the degree of the recuperative power of the organs and structures of the body, for these would materially alter the course and prognosis of the disease.

Also, the digestive system, if markedly depraved, would impede satisfactory improvement of the patient.

The heart is of paramount importance in consideration of the prognosis in Graves's disease. A heart which beats at 120, 140 and even 160 a minute is one which will rapidly give out through degeneration of the musculature.

The nervous system with its intricate ramifications and manifestations is of prognostic importance. This leads to a consideration of insomnia, gastric and intestinal neurosis, and bladder neurosis. The severity and duration of the disease as in other morbid processes influence the prospect of recovery. In general it may be remarked that an individual having suffered from this disease for from twelve to eighteen months, all things being equal, is fully capable of prompt recovery. A case of three or four years duration offers many difficulties, though not at all incurable by appropriate therapeutics.

The presence or absence of complications is here, as in other diseases a factor to be taken into account. The complications most usually encountered are mentioned above.

Emphasis is placed by Bram on the social condition of the patient. This will alter the course and the prognosis of the disease insofar as the proper quantity and quality of foods, hygienic surroundings and conservation of en-

ergy are concerned. The essential hygienic surroundings—such as proper care of the household, especially the chamber which the patient occupies—the matter of personal hygiene and its attendants, all these, if afforded, add to the grand total of beneficial progress.

The coöperation of relatives and friends is of great importance inasmuch as it bears directly on the mental poise of the patient. Also, the coöperation of the patient is highly desirable in treatment of this disease. One who promises to do everything and does little, will in course of time succeed in bringing about her end.

Of extrinsic factors considered important by Bram, the first mentioned is early diagnosis. Hyperthyroidism simulates closely many diseases commonly encountered. The marked emaciation, weakness, diminution of respiratory expansion, occasionally slight rise in afternoon temperature, and marked hyperidrosis, all of these in the absence of visibly enlarged thyroid gland and marked exophthalmos may direct the general practitioner toward a diagnosis of pulmonary tuberculosis. Again, the diagnosis of hysteria, neurasthenia, or hysteroneurasthenia, is made on the basis of the existing change in disposition, loss in weight, lack of appetite, irritability, insomnia, and occasional outbursts of emotionalism, such as temper, melancholia, crying spells and, at times, moments of mania or dementia.

It is the exception rather than the rule for the early stages of Graves's disease to present all the typical cardinal symptoms, that is, goiter, exophthalmos, tremor of the outstretched fingers and tachycardia.

The next question discussed is that of treatment, and the one decision to be made is: Shall the treatment be surgical or non-surgical?

In discussing this point, Bram emphasizes the fact that many patients who have been treated surgically for exophthalmic goiter are improved and not cured. The symptoms are relieved, but this is only temporary. In the rare instances in which there is no recurrence of the symptoms within a year or two following thyroidectomy the surgically treated patient has obtained either a natural cure, that is, the patient was one of those rare instances which tended toward spontaneous recovery.

treatment or no treatment, or the cure is a non-surgical one. The non-surgical treatment of exophthalmic goiter is in Bram's opinion the method to pursue in nearly every case. Even former enthusiasts of thyroid surgery, he maintains, are now beginning to realize the futility of operations and look with favor on non-operative measures. The proper medical attendance, the proper social atmosphere, and the right kind of dietetic, hygienic, medicinal, psychotherapeutic and other measures properly carried out for the required length of time will with few exceptions effect a cure in every case of exophthalmic goiter. The duration of treatment depends largely on the patience and perseverance possessed by the physician in charge, and bears strongly on the course and prognosis of the disease. As a general rule, Bram states that a case of two or three months' duration usually requires the same duration of treatment. One of a year's duration may require from eight to twelve months. A patient having suffered from hyperthyroidism for a year or two years is more difficult to bring around to a state of clinical recovery, for there has been established a habit of hyper-excitability of the circulatory and nervous systems.

In regard to where treatment should be carried out, whether at a hospital or in a home, Bram says that this can be decided only after careful study of the individual case. The hospital, though advocated by some as a routine procedure in this disease, is not a place of choice in the average case, unless the patient is menaced by an impending loss of circulatory compensation. The prime need of these patients is not the hospital rest cure with its associated milk diets, but an environment in which healthy people and normal circumstances abound, where appetite, digestion and assimilation will be so enhanced as to promote a progressive increase in weight and strength. In almost every instance, to remove the patient from her accustomed environment will, with an occasional exception, accentuate the nervous irritability and the nervous symptoms. He emphasizes, finally, that the personality of the physician can not be ignored as a factor in the course and prognosis of the disease in which psychotherapy is a constituent of the *régime*.

[There are toxic goiter patients who may be greatly

improved or entirely relieved by an adequate, efficient and rational medical management. When possible medical management should be tried primarily. If found impractical for individual patients, or if no satisfactory permanent improvement occurs in a reasonable period of medical management, operative management by an experienced capable surgeon should be carried out. The conscientious doctor will be guided also by good common sense.—B.]

**The Rôle of the Thymus Gland in Exophthalmic Goiter.** In an attempt to determine whether or not an excess of the product of thymus activity in circulating blood could cause exophthalmic goiter, experiments which are the basis of this paper were carried out by N. B. Eddy,<sup>9</sup> at McGill University.

Eight apparently normal rabbits were selected and divided into three groups. One group consisting of two rabbits served as a control, the remaining six animals received hypodermic injections of thymus gland substance at fixed intervals. One group of three rabbits was given the thymus substance in the proportion of 5 mg. per kilogram of body weight, and the remaining three in the proportion of 10 mgm. per kilogram.

During the course of the experiment, two of the rabbits became pregnant. During the period of eight weeks that the experiments lasted forty injections were given each rabbit. The routine procedure was as follows: Each rabbit in turn was removed from the cage, weighed, pulse-rate counted, width of palpebral fissure measured, the general condition of the animal noted with especial reference to glandular enlargement, and the proper dose injected. The results obtained are tabulated in the original article, and the author states that by reviewing the results of the experiment, he sees no evidence of the production of symptoms characteristic of exophthalmic goiter by the thymus gland substance employed. He states further that a review of the literature indicates that there is a connection between the thymus gland and exophthalmic goiter, but what the nature of this connection is has not yet been discovered. It is possible that the thymus acts independently of the thyroid in producing

(9) Canadian Med. Ass'n Jour., March, 1919.



Basedow's disease; excited to hyperplasia and hypersecretion by external influences, it causes the group of symptoms that constitute this disease. It is also possible that because of a dependent relationship between it and the thyroid it becomes hyperactive as the result of increased activity of that gland, adding its harmful influence to that exerted by the abnormally functioning thyroid; or, its hyperplasia and hypersecretion may be the result of an effort to render harmless the toxic products of the thyroid. Still another conception of the etiology of Graves's disease which must not be overlooked is that suggested by Crile, namely, that neither the thyroid nor thymus is primarily at fault, but that there is a third cause, which is unknown, and that the changes observed in these glands and the symptoms attributed to alteration in their function are the result of the operation of this unknown factor.

**Myxedema and Hypothyroidism.** Myxedema in its classical form is a rare disease; like many other uncommon diseases, it is very often unrecognized in practice, especially the less marked cases which are not so rare. As usual, lack of careful examination of the patient more often causes the error than lack of knowledge.

In his discussion of the condition, George Dock,<sup>1</sup> of St. Louis, points out that the thing to remember is that this condition may occur at any age, although most cases are discovered in infancy or in late middle life. It affects people of all occupations and of all degrees of financial want or independence. The essentials to recognition are a general knowledge of the symptoms, such as can be gleaned from any text-book, the application of this knowledge to all patients examined, the realization that hypothyroidism has been mistaken for various other diseases, and the differential diagnosis in all such cases.

Another valuable aid is found in therapeutics. In substitution therapy there is a touchstone for hypothyroid conditions which is of the greatest value, and when there is doubt as to whether edema or loss of memory, or skin affection, or menorrhagia is of thyroid origin, one has only to make a careful test, and the answer will be soon given. That there is danger in the test is not a serious

(1) Jour. Missouri State Med. Ass'n, May, 1919.

contraindication. The grèatest danger is in the few cases of hyperthyroid disease that may be lighted up by thyroid administration. These should always be suspected. If they are intensified it must be remembered that any accident, such as over-work, an infection like tonsilitis, or even emotional shock, might produce the same symptoms, and if the therapeutic test is carried out with the care it deserves no great harm can follow.

In discussing the diagnosis of this condition, the author refers to some of the common difficulties in practice and the way to avoid them. He refers first to the frequent mistake of treating myxedema patients for nephritis. The diseases may be combined and in many cases of myxedema there is a low grade albuminuria. But even in such instances, the hypothyroid element can usually be recognized with little trouble. The subcutaneous swelling, usually the basis for the wrong diagnosis, is rarely like the edema of a parenchymatous nephritis, or still less like that in interstitial nephritis with its characteristic cardiac features. The swollen lips, as well as eyelids, the tougher, even wooden hardness of the swelling instead of the soft pitting of nephritis, the dry rough skin with almost never failing pigment changes, should at once excite suspicion of something more than nephritis. The history of onset, if investigated, will show not only an absence of causes of nephritis but a wholly different and often most picturesque course. The blood-pressure is usually low, but may be high.

Between hypothyroidism and senility as between the former and the menopause, the study of the complete course and symptomatology should lead to at least a therapeutically useful diagnosis.

Changes in hair growth are among the most important symptoms. Some of these are similar to senile changes but they often occur before the usual senile age. Alopecia, especially at the edges of the hairy scalp, and alopecia of the body or extremity hair formerly present and before general senile changes are especially noteworthy.

Myxedema pads are often not present or not marked, and so may lead to a wrong diagnosis. There may be a distinct thickness of the subcutaneous tissue, local or gen-

eral and its rapid melting away under treatment sometimes gives the finish to a doubtful diagnosis.

An important symptom related to the skin is the sensation of coldness or the sensibility to cold with actual low internal temperature. This may be present in nephritis or cardiac dropsy, but in many hypothyroid patients it is easy to get a history of low temperature, or cold feeling many years before, sometimes life-long, and at any rate without cardiac defect. Itching, especially of the legs, so common in senility, is sometimes of hypothyroid origin.

When the various phenomena already mentioned have been observed, the thyroid region should be examined. The results vary widely. There may be no traces of a thyroid gland and no history of pain or swelling, or there may be a history of repeated throat infection. In some instances there is a goiter, either colloid or fibrous, and occasionally a clear history of thyroiditis, or strumitis, especially with or after an acute infection of some kind.

In the cases simulating nephritis and in many others, the mental changes are often important so that in all cases with mental alterations the thyroid must be investigated. Migraine which has been attributed to so many different causes is also thought by some to be of thyroid origin. Even in the presence of hyperthyroidism the author considers that other causes of migraine should be searched for.

The combination of paralysis agitans and myxedema has been reported by several observers. Menstrual anomalies are not uncommon in women with hypothyroidism and include all forms from amenorrhea to severe menorrhagia.

Rheumatic symptoms, especially arthritis, are often referred to hypothyroidism.

**The Prevention of Goiter.** That the prophylaxis of goiter, if earnestly attempted, would succeed in from 30 to 50 per cent. of cases, is the contention of Israel Bram.<sup>2</sup>

The chief preventable means are the boiling of water in regions where goiter is endemic, the favoring of a less fleshy and more iodine-containing diet, and the re-

moval of focal infections, especially of the mouth and intestines.

School children may be protected against goiter by the administration, under careful supervision, of iodine or the iodides.

During adolescence and pregnancy, thyroid disturbances may be overcome by the judicious administration of thyroid extract, the iodides, or both. Physical and mental repose are essential requirements.

The prevention of exophthalmic goiter is intimately related to the prophylaxis of simple goiter since (a) etiologic factors common to both toxic and non-toxic goiter may lead to primary Graves's disease, and (b) a simple goiter may become toxic during the course of its existence, leading to a secondary Basedowian syndrome.

The relaxation in the strenuousness of modern life, in favor of the simple mode of living, and reversion to the old-fashioned short engagement and to early marriages, would tend to reduce the number of cases of Graves's disease to a minimum.

Exophthalmic goiter being primarily a functional disturbance of the endocrine organs, in which the thyroid gland is made to saturate the blood with its secretion, resulting in a turbulency of the nervous, circulatory, and other functions, is not only largely preventable through the suggested prophylaxis but is also, non-surgically curable by the institution of the proper corrective, dietetic, hygienic and medicinal measures. Bram has succeeded in curing every primary case of Graves's disease that came to his attention, some of these patients having previously undergone thyroidectomy without benefit.

**Hyperthyroidism Without Exophthalmos.** The frequency of excessive thyroid secretion unassociated with exophthalmic goiter, the fact that many cases of true exophthalmic goiter have a medical side and can be relieved and cured without surgery, are points emphasized by W. F. Boggess<sup>3</sup> of Louisville, in a clinical study of hyperthyroidism.

He states that close watching and careful analysis of a large number of persistent tachycardias, unaccompa-

(3) Kentucky Med. Jour., April, 1919.

nied by any perceptible increase in the size of the thyroid glands, but with persistent disturbances of metabolism, loss of weight, and increased nervousness, will unearth a large number of unsuspected atypical hyperthyroids with the cardiovascular symptoms remaining in the ascendancy. While it is true that many of the atypical exophthalmic cases may merge into the typical complex, yet many do not, but occur and recur in exacerbations, the tachycardia showing in paroxysms as a result of hypersecretions from neuropathic shocks and tendencies, from some focal infection, or from disturbances of some of the other glands and organs of internal secretion in which the hormone equilibrium is disturbed.

The author refers to the typical goiter, and the symptoms that accompany it. This picture, he says, is easily recognized by any clinician. Concerning the etiology, he states that no single cause can always be demonstrable. Any change in the body that causes irritation in some domain of the vegetative nervous system, particularly local infection, such as sinus, tonsillar, pulmonary and digestive tract infections, unquestionably are frequent causes of thyrotoxic outbursts.

Bogges has observed the relationship between chronically infected tonsils and enlargement of the thyroid gland with thyrotoxicosis. Three of his patients who had well-defined Graves's disease were women between 20 and 30 years of age, with bad tonsils; when the tonsils were removed they entirely recovered and presented no further evidence of any thyroid intoxication.

In many atypical cases it has been found that by removing infected tonsils and by relieving infection in the post-nasal spaces, the patients have responded to the treatment; the health has improved and the cardiovascular symptoms have abated or ameliorated.

In the treatment of this condition, instead of treating symptoms, one should find the cause, which in many instances is a focal infection, and remove it. Rest in bed, sunlight, fresh air, absolute physical, mental and nervous rest, are factors to be emphasized. Forced feeding, with an eye to those positive metabolic activities that exist in these cases should also be carried out. The administration of iron and arsenic, preferably hypodermatically,



is considered by Boggess to be of great value. He gives 3 grains of sodium cacodylate every second or third day for a prolonged period; also, 5-grain doses of hydrobromide of quinine, and possibly the addition of ergot in 1-grain doses three or four times a day produce in many instances positive results. Lactate of strontium two or three times a day in full doses has produced good results in many instances. The rapid heart frequently is not affected by digitalis, in which case strophanthus should be used. In many instances these two drugs are combined by Boggess in order to accomplish the best results. When the two fail, tincture of aconite should be given in full doses—20 to 30 mm. three times a day may prove beneficial. The use of thyroid extract, of adrenalin and pituitary extract, hydrotherapy and electrotherapy, are mentioned. The first of these, however, is considered unwise. Insomnia can be controlled by the administration of large doses of strontium bromide in conjunction with small doses of veronal or similar drugs.

If patients presenting these conditions are studied with the idea of finding a cause as a focus of infection and removing this, and treating the symptoms as outlined above, it is the opinion of this author that from 70 to 90 per cent. can be relieved and cured.

**Relation of the Thyroid to Neurocirculatory Asthenia.** The statistics upon which this report is based were collected by the authors, Thomas Addis, and William J. Kerr,<sup>4</sup> of the Medical Corps, U. S. Army, who were members of the Cardiovascular Board at Camp Lewis, Washington.

The object of the investigation was to determine the relative frequency in recruits with and without thyroid enlargement of certain signs and symptoms which occur in neurocirculatory asthenia. A considerable number of soldiers under training were referred to the cardiovascular board on account of the presence of a certain syndrome, which included all or most of the following signs and symptoms: increased pulse-rate; tremor of the fingers and cold moist hands which became cyanosed when dependent; precordial pain with dyspnea and palpitation on moderate exertion; such indications of vasomotor

(4) *Archiv. Int. Med.*, March, 1919.

instability as dizziness, flushing and fainting, and a variety of other complaints, all pointing to a state of excessive reaction of the nervous system to psychic or physical strain.

The impression was gained that thyroid enlargement was almost constantly found in men with this syndrome. That they were not cases of exophthalmic goiter was at once evident. It is well known, however, that in certain instances of endemic goiter a toxic state develops which resembles the condition named above. Reference is made to the fact that at Camp Upton 75 per cent. of the men who presented this syndrome were found to have thyroid enlargement; at this camp the condition was attributed to hyperthyroidism. This investigation was carried out, therefore, to determine whether or not the signs and symptoms mentioned above were more frequent in recruits with thyroid enlargement than in those who had no thyroid enlargement.

In carrying out this work, recruits were divided into groups of those with certainly enlarged thyroids, those with possibly enlarged thyroids and about whom there remained some doubt, and those who had no enlargement of the thyroid gland and who were designated as non-thyroid. First, the study was made of certain isolated signs in the recruits with and without thyroid enlargement, and the first of these was increased pulse rate. This study included 143 men with certainly enlarged thyroids, 533 with possibly enlarged thyroids and 900 non-thyroids. The results are tabulated and it is shown clearly that thyroid enlargement in a group of individuals is not associated with any increases in the average pulse rate of the group.

It is also shown that thyroid enlargement in these men was not associated with any special type of pulse rate.

The study of tremors in this same group of men indicated a relation between thyroid enlargement and tremor. Tremor was three times more frequent in the group with certainly enlarged thyroids, and nearly two times more frequent in those with possibly enlarged thyroids than in the non-thyroid group. Other symptoms studied were cyanosis of the hands, curved nails, moist hands and dermatographia, and the conclusion

reached is that thyroid enlargement as seen in this group of men did not influence these symptoms.

The further symptoms that were studied were divided into three groups: dyspnea, palpitation and precordial pain are classed as cardiac symptoms. Dizziness, flushing and fainting are taken as indications of vasomotor instability. Mental irritability, emotionalism, apprehension, depression, excitability and exhaustion, and "shakiness" after exertion or excitement were all grouped under the heading of nervous instability.

The final conclusion drawn from this work is that so far as symptoms are concerned there is no appreciable distinction between the two groups. What has been termed the symptom-complex, that is, an association in the same individual of symptoms of cardiac, vasomotor and mental instability is as often seen in non-thyroid as in thyroid patients.

**The Relation of Neurocirculatory Asthenia to Hyperthyroidism as Determined by the Effects of the Injection of Epinephrine.** This paper deals with neurocirculatory asthenia and its possible relationship with hyperthyroidism. Many of the symptoms of neurocirculatory asthenia are said to be so similar to those found in hyperthyroidism that the theory that this condition is a latent or very mild thyrotoxicosis has often been advanced.

Goetsch employed epinephrine given subcutaneously, as a test for latent hyperthyroidism. The test, in short, consists of subcutaneous injections of 0.5 cc. of a 1:1000 epinephrine solution with subsequent observations of the pulse rate, blood-pressure, tremor, nervousness and throbbing of the blood vessels. A rise in pulse-rate and blood-pressure and an augmentation of the nervous phenomena indicate a positive reaction. A normal individual presents none of these changes.

Ernest P. Boas,<sup>5</sup> of New York, made a study of twenty-one patients who presented cardiac symptoms, and who were considered to be in the class of neurocirculatory asthenia, making this epinephrine test for latent hyperthyroidism. Chief among the subjective symptoms complained of by the patient who gave a positive

(5) *Archiv. Int. Med.*, October, 1919.

reaction in this study were precordial pains, vertigo, headaches, epigastric distress and nausea. Only six patients gave a positive reaction. Four of the patients with a negative reaction complained of slight vertigo. It is notable that only four of the twenty-one patients studied in this work had palpable thyroids and that only one of these gave a positive reaction. An analysis of the results obtained by this study indicates that it is impossible to predict from any of the criteria available at present whether or not any particular case of neuro-circulatory asthenia is sensitive to epinephrine or not. In a study of sixty-five patients suffering with neuro-circulatory asthenia, Peabody found positive reaction in 60 per cent. of them. In this smaller group, Boas found positive reaction in only 28.6 per cent.

It is pointed out further that typical eye signs of exophthalmic goiter are rarely if ever found in patients with neurocirculatory asthenia. The tremor in the latter disease is much coarser and, finally, in spite of the fact that the symptoms may exist for years, cardiac hypertrophy, such as is found in goiter is never seen in these men with irritable heart.

**The Basal Metabolism in Hypothyroidism.** This article is based on observations on six patients and includes practically every condition clinically associated with hypothyroidism, namely, myxedema, cretinism, cachexia strumipriva, and cancer of the thyroid gland. The effect of thyroid administration on the basal metabolism was studied over a long period of time in the case of a cretin and in one patient with myxedema, also in a patient with cachexia strumipriva, before, during and after the appearance of hypothyroid symptoms.

The methods employed consisted briefly in the determination of the gas exchange of the recumbent subject while in the post-absorptive condition by means of the small Benedict apparatus and the calculation of the heat production therefrom.

The work was conducted by J. H. Means and J. C. Aub,<sup>6</sup> of Boston.

The metabolism data are all shown in table forms, the figures for any one day being the average of at least

(6) *Archiv. Int. Med.*, October, 1919.

two, and usually three ten-minute periods on the Benedict apparatus. These figures are not included in the abstract for obvious reasons.

After extensive protocols are presented, there is included in the first portion of the discussion a brief *résumé* of similar work that has been done by others. The authors state that the observations in the present work conform in general to the findings that have been made previously. The three myxedema patients studied showed before treatment variations of 33 per cent., 25 per cent. and 18 per cent. below the normal for their age and sex. One cretin patient whose cretinism was regarded as a mild grade showed a reduction of 23 per cent. below the normal for a woman of her age. The one case of cachexia strumipriva is interesting, for after removal of the greater portion of the thyroid the metabolism was 14 per cent. below normal before any clinical manifestations of hypothyroidism were observed.

In the one instance of carcinoma of the thyroid there was a reduction of 19 per cent. in the metabolism before operation and of 17 per cent. after operation without definite clinical evidence of hypothyroidism.

Thyroid therapy was used with these patients, and concerning its effect the authors agree with Janney that small doses are better than large ones. In one instance of myxedema the metabolism was brought to normal and the symptoms of myxedema were cleared up by a course of from 6 to  $7\frac{1}{2}$  grains of thyroid extract daily over a period of about one month. Following this, after continuing with  $11\frac{1}{2}$  grains a day for a year a course of 3 grains for two months raised the metabolism 11 per cent. above the normal. However, when this patient was seen two years later, having been taking  $11\frac{1}{2}$  grains a day in the *interim*, the metabolism was 14 per cent. below normal. In one cretin a total of  $25\frac{1}{2}$  grains of thyroid extract a week restored the metabolism from 23 per cent. below normal to normal without untoward results. Then the continuation of  $11\frac{1}{2}$  grains daily for several months served to keep the metabolism from 19 per cent. to 10 per cent. above normal. Following this after a period of nine months without thyroid medication, it fell to 11 per cent. below normal. After a brief discussion of the other



cases in detail, the authors say that the clinical lessons to be drawn from these studies are as follows:

First, the level of the basal metabolism is a better index of the degree of thyroid lack than is the clinical picture; and, second, the proper dosage of thyroid preparation can be far more accurately gauged by following the effect on the metabolism than from the appearance of symptoms in the patient. The aim should be to bring the metabolism to the normal level and then find the minimum dose that will keep it there. Janney's method of using the nitrogen balance as a criterion is considered good, but it requires a metabolism ward and considerable time and care to make such studies. The basal metabolism on the other hand can be determined quite easily and requires not more than an hour's time. The procedure is especially easy if Benedict's new portable apparatus is used.

The authors agree with Janney that large doses of thyroid extract are to be avoided. For the initial treatment 3 grains a day should be sufficient to bring the metabolism to normal and after the normal level has been reached from 1 to 2 grains may be required to keep it there. The proper maintenance dose will vary in different patients, and should be decided by metabolism determination. The importance of following the metabolism in cases of hypothyroidism is emphasized by the fact that the results in this paper show that a lower metabolism, and, hence presumably a state of hypothyroidism may occur without clinical manifestations and also by the fact that by thyroid therapy the metabolism can be raised above normal without clinical evidence of thyrotoxicosis.

From the study of patients with *cacexia strumipriva* it is concluded that these may require larger maintenance doses than those with spontaneous hypothyroidism.

**Malignant Epithelial Growths of the Thyroid.** The classification of epitheliomata of the thyroid gland used by H. K. Bonn<sup>7</sup> is that given by Langhans, and is as follows: malignant adenoma, or proliferating goiter; metastatic colloid goiter; papilloma; para-struma; post-

(7) Jour. Ind. State Med. Ass'n, March, 1919.

branchial goiter; carcinoma; and caneroid or squamous-celled carcinoma.

The malignant adenoma is usually one small nodule with a lobulated surface, and quite commonly there is present a necrotic center, similiar to a scar. This growth is peculiar in the fact that its neoformed vesicles are lined with a single layer of epithelium containing colloid. The peculiar shape of the blood-vessels which are irregular, and the fact that the cells lie in direct contrast with the tumor cells, suggest a normal organ in a state of development rather than a cancer, according to Crotti.

Metastatic colloid goiter does not differ histologically from a simple colloid goiter, except in the distinctive feature of metastases formation, these metastases occurring by the vascular route usually, although they may occur through the lymphatics.

Thyroid papillomata are usually small in size and have a nodular form with a smooth surface, and the growth may be either solid or cystic. The tumor corresponds to the ordinary papilloma, and metastases occur through the lymphatic glands and present the same histologic picture as the primary tumor.

Para-struma is the glycogen-containing goiter described by Kocher, jr., and presents a nodular surface, grows rapidly, and quickly becomes adherent to neighborhood structures. The cut surface of such a growth is grayish-white.

Metastases from para-struma are found in the bronchial, mediastinal and cervical glands, and also in the bones. Post-branchial goiter grows rapidly and presents a grayish-brown or grayish red appearance on cut sections. Metastases are found in the liver, lungs and cervical glands from post-branchial goiter. Carcinoma of the thyroid is usually a hard nodular tumor, which is adherent to the neighboring tissues. Caneroid or squamous-celled carcinoma never reaches a large size, and is a rare tumor. This growth may occur in the normal thyroid as well as in pre-existing goiter. Caneroid always has a close connection with the pharynx and larynx, and it is believed by Langhans that this tumor has its origin in these structures, or in the remains of the thyroglossal duct.

Malignant diseases of the thyroid usually appear between the ages of forty and sixty years, and quoting Hertzler the disease develops in 90 per cent. of cases more frequently in females than in males.

The development of thyroid malignancy may be either acute, latent or subacute according to Crotti. For the acute type, three or four weeks may suffice to produce alarming symptoms of suffocation and widespread tissue infiltration. This acute form of malignancy is sometimes difficult to differentiate from acute thyroiditis. In the latent form, the thyroid is modified but slightly in size, form and consistency. Numerous metastases are found, however, this type is rare.

The most frequent form is the subacute type, in which cancer appears in a goiter which has been present in a stationary form for years. Apparently without cause the growth begins to enlarge and the consistency to change from soft to hard. These two physical signs are sufficient to cause the physician to suspect a beginning malignancy. Later, interference with respiration, occurs, the voice becomes rough, harsh and bi-tonal and swallowing becomes difficult. Pain running to the chin or ear appears shortly. The tumor becomes adherent to contiguous structures. A barking cough is frequently present and paroxysmal choking attacks may appear.

Thyroid insufficiency does not occur frequently, either because the entire gland is not involved as yet, or because the malignant thyroid cells have not lost their physiologic property.

## THE THYMUS

**Status Lymphaticus.** Experience with a single instance of status lymphaticus is recorded by E. L. Rice,<sup>8</sup> Medical Corps, United States Navy.

The patient whose record forms this report was a man 29 years old, a lieutenant in the Navy, who was and had been in good health when he was given 0.5 c. c. of standard United States Army typhoid bacterin containing parathyphoid bacilli *A* and *B*. The bacterin was given under the subcutaneous tissue of the left arm over the

(8) U. S. Naval Med. Bull., January, 1919.

deltoid. This injection was given about four o'clock in the afternoon, and without eating as much as usual for dinner that evening, the patient left the table and went to his room. Nothing more was seen or heard of him until the following morning when he was found dead in his bunk.

In a summary of the findings at autopsy on the body, it is stated that the lymphatic system showed hypertrophy and the thymus was very prominent. The heart, although dilated, was not larger than normal, and the whole arterial system had been dwarfed. An atheromatous change beginning in the arch of the aorta did not extend to the kidneys and the smaller vessels.

The exciting cause of death was the first injection of triple vaccine, but since it is known that the body tolerates well the foreign protein contained in dead typhoid and paratyphoid bacilli, there was no true anaphylactic reaction, and the cause of death was a toxemia, which might have, during the course of the next two or three months, been induced by any of the infectious fevers or follicular tonsilitis, with the same fatal results.

At the same time that this patient received the injections of typhoid vaccine, eighteen other men were given injections from the same ampoule, with no unusual symptoms or abscess formations, and since the bacterin was not cloudy, it is concluded that it was sterile. The portion remaining in the ampoule had been immediately discarded after the injections, therefore, no cultures could be made.

## THE SUPRARENALS

**Mesothelioma of Both Suprarenal Bodies and Both Lungs.** This report is based upon observations made in one patient by W. H. Harris,<sup>9</sup> of the Laboratory of Pathology, Tulane University, New Orleans.

By way of introduction he states that the uncertain derivation of certain tumors of the upper pole of the kidney and its adnexum, the adrenal, has caused many neoplasm which arise in these organs to be erroneously classed as hypernephromata. Omitting those tumors de-

(9) Amer. Jour. Med. Sci., May, 1919.

scribed by Grawitz as classical of the type hypernephroma, there remain many other distinct varieties of growths to which miscellaneous descriptive names have been applied. Unfortunately, many of these tumors, because of their occurrence in or about the hypernephric region, have been recorded as hypernephromata.

In the present consideration the occurrence of tumors in both adrenals and both lungs, identical in their histopathology and interesting in their cytologic picture, together with the interesting clinical picture, form the basis of this report.

The patient was a colored male, 48 years old. His symptoms dated to about five weeks previous to his entrance to the hospital, and consisted of a swelling in the right side of the chest, extreme pain in both sides of the chest, difficulty in breathing, and diarrhea. When examined by Harris he was found to have rapid and shallow respiration. There was flatness over the entire right chest, the left side was practically normal to percussion. Over the right lung, the voice and respiratory sounds were only barely audible. Over the left lung, scattered râles of the coarse and fine moist varieties were heard throughout.

The right pleural cavity was aspirated and blood was drawn. The patient died one day after he was admitted to the hospital and a clinical diagnosis of bilateral pulmonary tuberculosis with right hemothorax was made.

At autopsy the right pleural cavity was found filled with a dark brown fluid which was thought to be partly hemolyzed blood. The right pleura was studded with small nodular areas which gave the appearance of dark skin and appeared tuberculous in character. The left pleural cavity was dry. The left lung was dark gray, and studded on the surface with small grayish nodules. The entire lung was very nodular. On sectioning, the organ presented throughout small yellowish white and grayish white masses from 2 mm. to 2 or 3 cm. in diameter, the larger areas presenting necrotic central portions. The right lung presented a similar aspect, but the nodules were more numerous and in certain areas they coalesced. The surface of the pericardium internally and the surface of the



epicardium were studded with small grayish nodules which were rough and nodular on palpation. The left suprarenal gland measured 3x6 cm. An oblong body more or less caseous was found in it, this nodule presenting the appearances of a tuberculous lesion. The right suprarenal measured 3x4.5 cm. It presented on section a yellowish mass which filled up the whole section of the organ and measured 1 cm. in diameter. The diagnosis made at first was that of pulmonary and pleural tuberculosis, pleural hemorrhage and tuberculosis of the adrenals. By microscopic examination, however, the suprarenals were each found to contain neoplasms. These were separated in part from the gland by a connective tissue capsule, but farther on the tumor cells merged directly into those of the gland, extending through the zona glomerulosa, into the zona fasciculata, and in certain areas a few tumor cells invaded through zona reticularis into the medullary portion. In this area, the growth extended directly to the blood-vessels and although no embolic tumor cells were seen in the vessel lumina, metastasis *via* the vessels was suggested.

Sections of the tumor from both lungs showed numerous metastatic areas varying greatly in size.

The cytologic features of tissues from each lung were the same as those of the tumor in the adrenal. Microscopic study of the other tissues showed nothing of interest with the exception of the pericardium, which presented distinct tuberculous lesions.

In this case, the term mesothelioma has been employed by Harris, thinking, as suggested by Adami, to avoid confusion with Grawitzian hypernephromata and again as indicating its probable histogenesis.

**The Effects of a Scorbutic Diet on the Adrenal Glands.** A study of this problem was carried out by R. McCarrison,<sup>1</sup> by feeding guinea-pigs on a dietary of crushed oats and autoclaved milk. The naked-eye changes consisted in enlargement of the adrenals with increase in their weight and in congestion.

The weight of the adrenals in guinea-pigs dying in consequence of the scorbutic diet is approximately double that in health.

(1) Brit. Med. Jour., Aug. 16, 1919.

The histopathologic changes are hemorrhagic infiltration and disintegration of the cellular elements of the cortex and medulla. These changes occur in animals which may exhibit no clinical evidences of scurvy during life. They are to be regarded as pre-scorbutic in character. The areas of hemorrhagic infiltration are circumscribed and are situated around the periphery of the adrenal cortex.

The adrenalin content of the suprarenals of guinea-pigs fed on a scorbutic dietary was estimated in five animals by the method of Folin, Cannon and Dennis.

It was found that in spite of the fact that the weight of the organs is more than twice as great, the total quantity of adrenalin in a guinea-pig fed on a scorbutic diet is less than half that in healthy guinea-pigs.

Attention is directed to the fact that the total adrenalin per gram of gland in healthy pigeons is approximately ten times greater (0.0023 grams.) than in the healthy guinea-pig (0.00023 gms.) This greater proportion may bear some relation to the fact that uric acid is excreted as such in *aves*. A further point in connection with these results in guinea-pigs is the contrast they afford to the great increase in the adrenalin content of the adrenal glands which occurs in pigeons wholly deprived of accessory food factors of all classes. It has been found that the adrenalin content of these organs in *aves* is largely dependent on the class of accessory food factors which is absent from the dietary. When, for example, fresh butter, which contains accessory food factors of the "A" class, is added to a dietary of autoclaved rice, the adrenal glands of pigeons so fed do not, as a rule, contain an amount of adrenalin out of proportion to that found in health; exceptions occur in approximately 10 per cent. of all pigeons so fed. Nevertheless, the evidence so far available, both in birds and mammals, points to the dependence of the functional perfection of the adrenal glands on the adequate provision in the food of accessory food factors of all classes. It appears that lack of factors of the "A" class with excessive production of adrenalin is associated with the occurrence of edema in *aves*, and that in guinea-pigs lack of factors of the "C"

class with diminished production of adrenalin, is associated with hemorrhage into the body tissues.

**Tuberculosis of the Adrenals Without Bronzing.** K. Motzfeldt<sup>2</sup> calls attention to the fact that Addison, in his classical description of the disease associated with his name, put discoloration of the skin at the end of the list of distinctive symptoms. Yet this discoloration has come to be regarded as the most essential characteristic of Addison's disease. The following case shows how slight the discoloration of the skin may be even in a case terminating fatally, and it is also instructive as showing that, contrary to the generally accepted view, the carbohydrate tolerance may be very low.

A woman, aged 43, of tuberculous ancestry, had been treated for a year in hospital for spinal caries when she was about 20 years old. Since the age of 33 she has been suffering from attacks of abdominal pain, which at times had been severe enough to confine her to bed. At the age of 43 she suddenly developed headache, vomiting, and diarrhea, for which she was admitted to the hospital. She was pale and flabby, and the pulse was very small, otherwise the examination was negative. The diarrhea soon stopped, but the headache, nausea and vomiting persisted. After a short time in the hospital it was noticed that the backs of the hands were a trifle more brown than normal, otherwise there was no abnormal pigmentation of the skin and mucous membranes; this slightly dark tint of the hands did not deepen in the further course of the case. Asthenia and debility increased, the eyes were sunken, and the radial pulse was rapid and small often being barely palpable. The blood-pressure (Riva-Rocci) varied from 60 to 90 mm. of mercury. The temperature was uniformly subfebrile. She vomited a large proportion of the 100 grams of grape sugar given in 250 c.c. of tea, yet the urine for from two to five hours after contained 0.5 per cent. of sugar. Adrenalin given by the mouth proved inert; injected hypodermatically three times a day for several days, the dose being 0.5 c.c. of a 1:1000 solution, it appreciably reduced the lassitude and nausea; the pulse also became stronger. Control saline injec-

(2) Norsk Mag. f. Lægevidensk., April, 1919.

tions were negative. With the cessation of the injections she quickly relapsed, and died a few weeks after admission to the hospital with signs of progressive marasmus.

The diagnosis of Addison's disease was confirmed by the necropsy, which showed bilateral caseous tuberculosis of suprarenal bodies, not a trace of the normal suprarenal tissue being demonstrable, even on microscopic examination. The tuberculosis was strictly confined to the suprarenals, and there appeared to be nothing wrong with the other endocrine glands. Gall-stones were found, as well as considerable pigmentation of the mesentery and the mucosa of the intestines.

The author suggests that this case bears out Neisser's contention that melanoderma is a manifestation referable to the sympathetic system, and conspicuous by its absence when the disease is strictly limited to the suprarenal bodies.

**Traumatic and Tuberculous Lesions of the Suprarenal Capsules.** In a study of ninety autopsies conducted during the course of the war William T. Goormaghtigh<sup>3</sup> describes three cases of traumatic lesions of the adrenals in this series and four of tuberculous lesions. In the first case of traumatic injury of the adrenal, hemorrhage was pronounced, without gross lesions, but the microscopic picture showed hemorrhagic areas in the cortex and throughout the medulla. The case cited followed a large retroperitoneal hematoma as a result of a bullet wound. The second case recorded showed marked destruction of the cortex of the adrenal associated with trauma of the spleen and the kidney. In the third case, there was a large hematoma of the right adrenal which destroyed the cortex and a large area of the medulla. This occurred in an old man who suffered from a basal fracture of the skull. The author thinks that injury to the adrenals sometimes occurs in crushing injuries or violent traumata involving the thoracic vertebrae, and the abdominal walls, and that in old persons hemorrhage in the adrenals is frequently found in cases of injury to other parts of the body due to the abundant arteriovenous supply and the relative

(3) Presse méd., February, 1919.

large size in old age. However, the rapidly fatal termination was easily accounted for by the other traumata. In the tuberculous lesions of the adrenals, three of the soldiers who succumbed from wounds presented unilateral involvement but there was no clinical evidence prior to autopsy to suggest this condition.

In the fourth case there was marked fibrosis of the adrenals which affected the upper part of the gland, and had destroyed the medullary portion. The rapidly fatal termination was not accounted for by the associated wound of the lower extremity but was ascribed by the author to the involvement of the adrenals. The symptoms of adrenal insufficiency presented were the peculiar variety of shock, sudden marked lowering of the blood-pressure, followed by complete disappearance of the pulse, vomiting, and pronounced agonal convulsions. The author suggests that adrenal insufficiency should be considered in certain varieties of traumatic shock.

## THE HYPOPHYSIS

**The Pituitary Gland and Diabetes Insipidus.** From the Bland-Sutton Institute of Pathology, Middlesex Hospital, London, there comes a report by E. K. Kennaway and J. C. Mottram,<sup>4</sup> of observations upon two cases of diabetes insipidus, with an account of the literature relating to an association between the pituitary gland and this disease.

The first patient whose record is presented was a man 22 years old, who about the end of June, 1915, was accidentally stabbed with a bayonet in the lower part of the left orbit. The wound healed in a week, while the eye remained bloodshot for a fortnight. The man noticed considerable thirst on the evening of the day that the accident occurred and it was quite certain that the thirst and polyuria dated from this day. Complete blindness of the left eye followed the accident.

When seen by the authors, the patient complained of weakness, loss of flesh, thirst and polyuria. The Wassermann reaction was negative. The fundus of the right eye was found to be normal and the left disc completely

<sup>(4)</sup> Quarterly Jour. Med., April, 1919.



atrophic. There was no perception of light in the left eye. Skiagram of the head showed abnormal smallness of the pituitary fossa.

During the first four weeks in the hospital, the volume of urine increased from about 3 liters to 7 or 8 liters daily. Administration of a pituitary preparation by the mouth caused no improvement.

During a given period the intake of protein and salt was diminished in the hope that the excretion of smaller amounts of urea and chloride would lessen the diuresis. By this kind of management the day's output of nitrogen and chlorine, which was already low, was reduced to about one-half, and after some days the volume of urine fell from about 8 to about 6 liters. As the daily excretion of nitrogen on this *régime* was only 4 grams, so that no further reduction could be expected, and that of chlorine about 2 grams, or about one-fifth the output of a person on ordinary diet, it was evident that no great success attended this form of treatment.

From this time onward, it became evident that the patient was recovering. The volume of urine fell from 2 to 3 liters daily, and its concentration increased. The patient was discharged soon afterwards at his own request, and the subsequent history is not known.

It is possible that the wound in the orbit in this case caused some disturbance in the region of the pituitary, perhaps by hemorrhage and thrombosis extending along the cavernous sinus. The immediate onset of thirst and polyuria is very reminiscent of Cushing's account of the effect in dogs of removal of the posterior lobe of the pituitary or division of its stalk. Probably some further complication occurred in the patient under consideration, since when he first came under observation two months after the injury the polyuria was of only moderate degree, 3 liters daily. Thereafter the volume of urine showed a well-marked wax and wane.

The second patient whose record is presented was a woman, 54 years old. Ten years previous to the onset of her present trouble she had noticed a lump in the left breast. This increased in size very slowly and was amputated about two years before she was first seen by the authors. Microscopic examination showed the growth to

be a carcinoma. About fifteen months after operation fresh nodules appeared in the right breast, the neck and under the arm.

The patient complained of loss of weight at the time she was admitted to the hospital, of weakness and of great thirst. The volume of urine was from 7 to 8 liters daily. The Wassermann reaction was negative. No recurrence of the tumor was seen at the site of operation. Subcutaneous nodules of growth in the right breast, right axilla, right and left supraclavicular fossae and midsternomastoid lymph glands and around the umbilicus were observed. There was no indication of pituitary involvement in the ocular condition. A diagram of the head showed a shadow one inch in length and one-half inch in depth situated about one-half inch above the sella turcica.

In this case the specific gravity of the urine was never observed to be below 1,002.

The treatment of the patient consisted at first in placing her upon a diet poor in protein and without added salt. The nitrogen and chlorine of the urine were by this means reduced to about one-half and the volume of urine fell from almost 9 to 5 liters, but it soon rose again to 7 liters.

The patient was given 1 c.c. pituitrin by mouth twice daily for eight days. This had no appreciable effect on the polyuria, but when the extract was given subcutaneously, the volume of urine was reduced by a single injection to about one-half, and the specific gravity raised from 1,003 to 1,006 or 1,007. Subsequently, the urine was collected over short intervals after the injection. During the first two hours a practically normal urine of specific gravity 1,014 to 1,016 was secreted, and the hourly volume rate was about one-quarter of that for whole day. The effect was still noticeable up to the ninth hour after the injection.

In order to investigate further the remarkable anti-diuretic action of pituitary extract, control observations were made upon a person showing no abnormality of the urinary secretion. An effect of exactly the same type was observed.

From this study it was found that the subcutaneous

injection of pituitary extract causes a diminished flow of urine for several hours; later this is compensated by an increased flow, so that the twenty-four hour's output may be unaltered.

The injection of a moderate amount sometimes causes an immediate decrease lasting for from ten to twenty minutes.

In cases of diabetes insipidus, the injection of pituitary extract causes antidiuresis as in the normal body.

Given by the mouth the extract is ineffective, but fresh gland given by the mouth is stated to be effective (Motzfeldt).

Anterior lobe extract has no effect on the secretion of urine.

In a final division of the work, some methods of treatment in diabetes insipidus are described.

First, antisymphilitic treatment must be employed when indicated by a positive Wassermann reaction, or other features of the case.

The most effectual treatment in other cases is, of course, the subcutaneous injection of pituitary extracts: the results to be expected are indicated above. The obvious disadvantage of this method is the necessity for daily repetition of the injection: instances in which a lasting effect has been ascribed to the treatment are no doubt to be explained by the independent recovery of the patient as happened in the first of the cases mentioned in this article. In the second patient studied in this work the subcutaneous injection of 1 c.c. of pituitrin produced a practically normal condition of the urine lasting about six hours, the beneficial effects being moreover still distinct during the next six-hour period. If then an injection were given at bedtime, and an uninterrupted night's rest should be secured, time must be allowed for the action of the bowels, which may occur. There seems to be no danger of any considerable rise of blood-pressure following injection of amounts sufficient for the purpose in question.

In a summary of this rather lengthy paper, the authors state that when large amounts of sodium chloride are given to patients with diabetes insipidus the diuresis is so adjusted that the percentage of nitrogen plus

chlorine in the urine remains unaltered; the kidney, therefore, lacks the power of concentration which is exhibited normally after ingestion of salt.

The antidiuretic effect of pituitary extract given by subcutaneous injection was demonstrated both in a normal subject and in a case of diabetes insipidus; administration of such preparations by the mouth is ineffectual.

No record has been found in the literature of any case of diabetes insipidus in which abnormality of the pituitary was excluded with certainty by postmortem examination, whereas, in a considerable number of cases the disease has been associated with a lesion of the posterior lobe of the gland. However, such lesions are not invariably accompanied by diabetes insipidus. The evidence of morbid anatomy as to a connection between the pituitary gland and diabetes insipidus is therefore inconclusive.

The experiments of Cushing have shown that polyuria can be produced experimentally by lesions of the posterior lobe of the pituitary, but the great variations in the duration (two days to six months) of these polyurias show that there is some very important factor which has not yet been determined. The polyuria produced by lesions of the brain adjacent to the pituitary (Camus and Roussy) may perhaps be accounted for by the diffusion of pituitary secretion in the brain substance. There is also some evidence that the polyuria following stimulation of other parts of the nervous system (medulla, superior cervical ganglion) is due to activity of the pituitary.

The antidiuretic effect of pituitary extract appears to be due to direct action on the kidney (Konschegg and Schuster); the experiments of Rees do not demonstrate that it is the result of diminished absorption from the intestine.

The immediate restoration of a normal state of the urine when pituitary extract is given in diabetes insipidus the strongest evidence for the normal activity of the gland in regulating the secretion of urine.

## THE PINEAL GLAND

**The Function and Clinical Uses of the Pineal Gland.**

The function and clinical uses of the pineal gland are discussed by W. N. Berkeley.<sup>5</sup> Long ago the view was advanced that the pineal gland, anatomically, is only a vestigial remnant of a third eye, occipitally situated, and still to be observed in certain reptiles.

The opinion is constantly gaining ground now among clinicians that physiologically it is a true organ of internal secretion.

v. Hochwart reported autopsy findings in which a cellular tumor of the pineal gland was found. He and his colleagues advanced the view that the pressure of this tumor had inhibited the growth and secretion of the pituitary. Berkeley takes the view, however, that the pineal secretion itself by reason of its increased amount brought about the extraordinary mental and somatic growth described in the case reported.

Working upon this hypothesis for several years Berkeley and his associate Dana were able to show that preparations of pineal gland obtained perfectly fresh from calves and young cattle, accelerated the somatic growth of kittens, rabbits and guinea-pigs to a marked degree, and that a number of backward children, without organic stigmata, to whom the gland was administered for a fixed period, usually from three to six months, made an advance in mental age considerably in excess of any previous progress for a like period. McCord was able to confirm this fully and to amplify feeding experiments. Various workers have obtained a variety of results by the removal of the gland. The later work of the author with the gland in backward children in private practice has continued to be gratifying and satisfactory. The only requirements are that the child shall be properly cared for in an educational way, and that the remedy should be continued for a long period, perhaps years instead of months and weeks.

Repeated careful and complete examination of children who are mentally subnormal will usually make it evident to the attentive student that glandular defi-

(5) Med. Record, Jan. 3, 1920



ciencies often do not come singly, and pineal gland must often be tentatively combined with other secretions. Minor grades of hypothyroidism should be specially suspected, and a dry skin, cold extremities, obstinate constipation, excessive mental hebetude, irregular and imperfect eruption of the milk teeth, low blood-pressure—one or all of these may be remarkably intractable, till thyroid is added to the formula. When the physical as well as the mental growth is retarded and there are changes in the size of the sella, or increased carbohydrate tolerance, or great obesity, or a systolic blood-pressure below 50 mm., the anterior or the middle part of the pituitary, or both, should be added. When the patient is a boy and has very minute and soft testes (a common occurrence) testis should be given. Sometimes several of these conditions coincide, and a pluriglandular formula of pineal, pituitary, testis (or ovary for girls), and thyroid—all in minute doses—may be tried, often with the most gratifying results.

If reliable results are to be obtained in diagnosis or treatment, the physician must not be satisfied with any gland preparation unless he is sure it is absolutely fresh and obtained from a well-known and reliable source. As a means of speeding up the sluggish cerebral chemistry of many backward children, Berkeley thinks that pineal gland will ultimately become a standard remedy; but the cases must be selected with reasonable care; permanent organic damage to the child's brain is usually an absolute contraindication.

He also believes that in premature decay of the mental powers in old people, this preparation will quicken the slowed-down, mental processes of old age, improve the memory, and produce a remarkable cheerfulness and sense of well-being.

## THE LYMPHATIC GLANDS

**Treatment of Hodgkin's Disease.** During a period of six years, C. F. Burnam,<sup>6</sup> of Baltimore, has treated more than one hundred patients who had Hodgkins'

<sup>66</sup> Surg. Gynec. and Obstet., May, 1919.

disease and malignant lymphoma or lymphosarcoma, which resembles it so closely clinically.

The importance of an exact diagnosis as a preliminary to adequate treatment is emphasized, and such diagnosis is said to rest on *x*-ray, blood and tissue examinations, as well as on a careful general physical examination.

In the advanced stages, the tissue examination is the

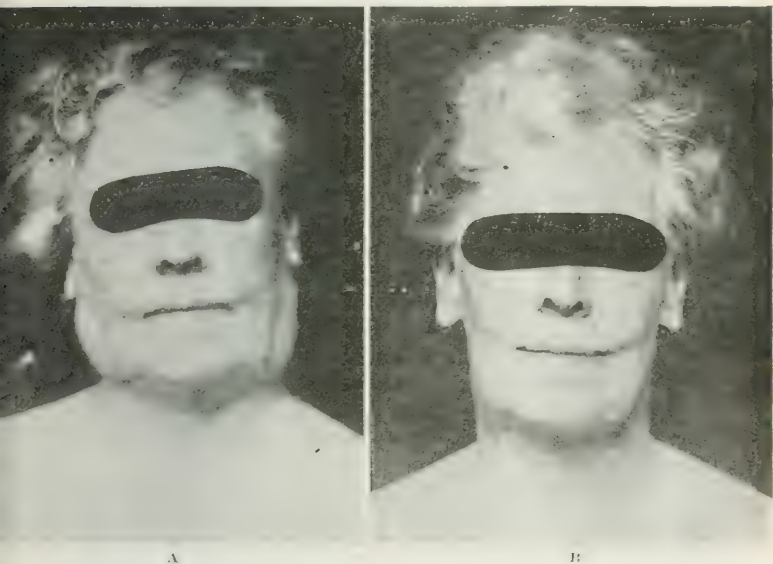


Fig. 17. A.—Hodgkin's disease with general involvement and marked pruritis. Before treatment.

B.—Same patient after three radium treatments. Complete disappearance of all evidence of trouble. Well at present. Cure has lasted more than three years.

most reliable single criterion. By this method Hodgkin's disease, lymphosarcoma, tuberculosis, syphilis and the metastatic tumors are readily separated. As a routine diagnostic measure, the author advocates the removal of at least two isolated glands.

Blood examinations are relatively much less valuable than tissue examinations. Out of thirty-four instances in which the tissue showed positive Hodgkin's disease,

the blood was positive in only twenty-one, and was negative in fifteen. Also, out of twenty-six cases in which the tissues showed positive lymphosarcoma, three presented the blood picture which Bunting has designated as characteristic of Hodgkin's disease.

Roentgen-ray examinations are considered by Bunting indispensable in determining the mediastinal and



Fig. 18. A.—Chronic Hodgkin's disease with extensive involvement of skin and clavicle, and infiltration of breast. Before treatment.

B.—Same patient after ten exposures to radium and still under treatment. At present her arm is greatly swollen but her general health is good.

chest involvement. They frequently prove the presence of marked trouble, when neither the history nor the ordinary physical examination suggests it.

While many of the patients referred to in this work were treated both operatively and with the x-ray, the author has made use of radium only combining it in some instances with rest in bed, forced feeding and iron in the

form of Blaud's pills. Most of the patients were in advanced stages of the disease. Many of them were acute cases, some of them practically *in articulo mortis*.

In general, better results have been obtained in cases in which the tissue examination showed lymphosarcoma than in cases in which it indicated Hodgkin's disease, and in Hodgkin's disease when the characteristic polymorphonuclear leukocytosis was not present. Chronic cases are more favorable than acute. Intensive prolonged exposures extending over long periods were found very satisfactory in some chronic cases were found not suitable in acute cases.

In a chronic case limited to one set of glands, a single exposure may lead to a cure, which has in one instance extended over five years. Heavy exposures in acute Hodgkin's disease are usually followed by rapid reduction in the size of the gland masses, but with no corresponding improvement in the blood or the patient's general condition. In these acute cases, rest in bed, forced feeding and mild fractional radiation are indicated. The most unsatisfactory chronic cases are those with very little glandular involvement but with marked constitutional symptoms and changes in the blood. In every case in which the infection is limited to isolated groups of glands, such as one side of the neck and axilla a complete disappearance of the gland can be looked for with confidence.

In chronic Hodgkin's disease, disappearance of the gland masses is almost invariably accompanied by an improvement in general health, gain in weight, disappearance of pruritis and the return of the blood to a normal appearance.

The guide to treatment is to be found in the effect on the gland masses, the blood, and the appetite and the general health in the individual case.

The author feels confident that permanent cure may be looked for in an increased proportion of these patients with further improvement of the radium method of treatment.

Excluding all patients in whom apparent cure has been less than three years, there have been two patients in whom lymphosarcoma was diagnosed who have been

perfectly well and without signs of trouble for more than five years. Four patients have been apparently well for over three years.

Excluding all patients in whom apparent cure has been less than three years there has been one patient with mediastinal and neck involvement in whom Hodgkin's disease was diagnosed, well for four years, and two patients well for more than three years. One of these had neck, axilla, groin and iliac glands, the other groin, axillary, neck and mediastinal involvement.

The author suggests that while there is no objection to the complete surgical removal of a localized group of glands, if it is followed by radiation, it does not seem to him that this is necessary.

Photographs of two patients, taken before and after treatment with radium are shown in Figures 17 and 18.



## DISEASES OF METABOLISM.

### DIABETES MELLITUS.

**Control of Acidosis in Treatment of Diabetes.** This paper is presented as an outline of the procedures developed in the management of diabetic patients at the clinic of the Rockefeller Institute for Medical Research, New York.

The procedure consists first of ascertaining the individual reactions of the patients in regard not only to carbohydrate tolerance, but also the tendency toward acidosis; secondly, of guiding the treatment by the metabolic reactions that have been ascertained.

The paper is published by E. Stillman,<sup>1</sup> who states that the minimum laboratory control with which satisfactory results may be considered possible consists of qualitative glucose and aceto-acetic acid tests on the daily urine samples, with determination of plasma bicarbonate when the urine shows a strong test for aceto-acetic acid, or when any of the clinical signs are unfavorable. The symptoms of incipient acidosis are extremely variable; they may include definite malaise, headache, slight nausea, neuralgic pains, or almost any abnormal symptoms. Consequently, the slightest unfavorable clinical sign at any stage of treatment should be taken as an indication for determining the plasma bicarbonate.

The outline of routine management of these patients includes first, the preliminary observation diet. On admission to the hospital, patients not suffering from acidosis are placed on the following observation diet in order to ascertain their behavior under standardized conditions.

#### OBSERVATION DIET.

Protein Gm.	Carbohydrate Gm.*	Fat. Gm.
1.5 per kilogram	10-25	Sufficient to bring total calories to 35 per kilogram body weight.

\* Carbohydrate in the form of green vegetables only, from 10 to 25 gm. according to the apparent severity of the case.

(1) Archiv. Int. Med., October, 1919.

Acidosis of the severe or moderately severe type (plasma bicarbonate  $\text{CO}_2$  below 40 volumes per cent.) has been considered the one contraindication to placing the patient on the observation diet and maintaining him on it for the usual length of time. Such patients are put on fasting directly on admission to the hospital as requiring immediate and active treatment.

The second step in this management consists in creating an aglycosuric state by continuous or intermittent fast. After the period of the observation diet, the patient is placed on a continuous fast. This is continued until the patient is rendered aglycosuric unless acidosis develops. By the continuous fast is meant absolute abstinence from all foods containing any demonstrable amount of carbohydrates, protein or fat, continued without interruption until the patient has been made sugar-free for twenty-four hours. In the author's experience, patients required from two to eleven days for this to be accomplished. Fluids in the form of clear soup, coffee and water are given daily in a total amount of at least from 500 to 2,000 c.c.

Stillman noticed that patients on continuous fast must be watched carefully for development of dangerous acidosis, as indicated by aggregate daily determination of plasma bicarbonates. Patients developing or retaining acidosis on a continuous fast are given intermittent fasts to accomplish the same purpose as the continuous fast. The manner in which the continuous and intermittent fast treatments are applied is governed by the state and behavior of the bicarbonate reserve in the blood.

In cases of no acidosis or only mild acidosis, as determined before the institution of fasting, a moderate fall in the plasma bicarbonate is permitted before the continuous fast is abandoned for the intermittent fast. If the existing acidosis is moderately severe (plasma bicarbonate  $\text{CO}_2$ , or from 30 to 40 volume per cent.) even a drop of 2 or 3 volumes per cent. in bicarbonate, especially if the fall be progressive, is sufficient to cause interruption of the fast.

In cases in which the bicarbonate determination shows a severe acidosis (plasma bicarbonate  $\text{CO}_2$  below

30 volume per cent.) active treatment is instituted as follows:

Sodium bicarbonate: 3 gm. per hour, dissolved in cold water, until the bicarbonate of the blood becomes normal.

Fluids: Forced to the limit, but not to the extent to cause nausea; an attempt is made to give about 5,000 c.c. of fluid during the twenty-four hours.

Clear, very strong coffee is given to the quantity of from 1,200 to 1,500 c.c. daily. Whisky has been found to produce evil rather than a good effect, and is therefore omitted. Active catharsis by calomel and salts, together with high colon irrigations until the washings are returned without fecal matter, are instituted.

The diet consists of from 6 to 800 calories in the form of eggs and lean meat. In the treatment of acidosis it has been found that nausea is the condition above all others to be avoided, because if this becomes uncontrollable, the successful treatment of the acidosis becomes almost impossible. Nausea may be produced by any one of the measures mentioned above, such as bicarbonate therapy, the forcing of fluids, catharsis, the institution of fasting, or the institution of feeding. At the very first sign of any intensification of nausea, the offending factor in the treatment is discontinued until the symptoms of nausea disappear.

The next step in this management is the estimation of individual carbohydrate tolerance on a diet of green vegetables alone. After the patient is made aglycosuric by the fasting method and has remained aglycosuric for twenty-four hours, he is placed on a graduated carbohydrate tolerance test. This test is performed by giving a diet of green vegetables alone, starting the test with green vegetables containing 10 gm. of carbohydrates and increasing the amount of carbohydrates 10 gm. each day until glycosuria results. Occasionally a trace of sugar is found to occur in the urine during the first days of the test. This not infrequently is found to clear up without fasting and the patients frequently show an ability to metabolize many times the amount of carbohydrate that the first sugar reaction seems to indicate as the limit of their tolerance. Therefore, on the first appearance of

glycosuria the amount of carbohydrate in the diet is not changed for another 24 hours. If at the end of this time there is a cessation of the sugar excretion, the test is continued, the carbohydrate food being increased daily until glycosuria appears on two successive days. This point is considered as indicating the carbohydrate tolerance of the individual under observation. Fasting is then again instituted until the patient becomes sugar-free for twenty-four hours. The determination of the maintenance diet is then begun.

The carbohydrate tolerance test establishes a basis for comparison with later tests, whereby the progress of the patient can be determined, and also affords a basis for the initial maintenance diet as described elsewhere.

In cases in which although acidosis has benefitted by fasting it is not entirely eradicated, the carbohydrate test diet has usually raised the blood bicarbonate to a full normal. The ketonuria which usually accompanies subnormal blood bicarbonate is diminished or entirely stopped. The green vegetable diet may be considered almost a specific for mild acidosis.

The next step in the management consists of a determination of the maintenance diet. By this diet is meant the mixed one, which is as near a normal diet as can be tolerated without glycosuria and with fully normal plasma bicarbonate. After having made the patient aglycosuric and having determined the carbohydrate tolerance, it is the custom to place such patients on a trial maintenance diet.

#### THE TRIAL MAINTENANCE DIET.

For 24 hours.

Carbohydrate	Protein	Fat
One-tenth the amount tolerated on the carbohydrate tolerance test.	1.5 gm. per kg. body weight.	Sufficient to bring the total caloric value of the diet to 25 calories per kg. of body weight.

If the diet is well tolerated and the patient appears to need more, an increase is made in the constituents which appear to be most needed. Care is taken that only one of the three constituents, either the fat, the protein or

the carbohydrates, is increased at a time, and in a gradual systematic manner, so that should glycosuria or ketonuria result the offending food could be recognized and reduced.

Urinary tests for glucose and ketones are made daily while the plasma bicarbonate is being determined at least once a week and as often after as the patient's symptoms render advisable.

When either glycosuria, definite ketonuria, or significant fall in plasma bicarbonate occurs on the maintenance diet, the patient is put on the so-called minimum maintenance diet, which is made up exactly as the maintenance diet, except that the fat is cut down so that the patient receives only 25 calories per kilogram of body weight instead of 35. Prolonged feeding (for from four to twelve weeks) of a diet of such low caloric content has frequently resulted in increased food tolerance so that the patient can finally take the maintenance or even more than the maintenance diet. When it is found possible to create such a tolerance, the patient is discharged on the lower diet.

Diabetic patients are divided into four groups previously described by this same author. These groups are marked by characteristic differences in their tendencies towards acidosis which are briefly summarized as follows:

The percentage given at the first of each group in the following statement indicates the percentage of patients studied in this work.

Group 1.—46.8 per cent. of cases: No tendency to acidosis, either on fast or ordinary diet, regardless of degree of glycosuria.

Treatment: Made aglycosuric without danger by continuous fast. Can usually be made to tolerate high calory diet without glycosuria or ketonuria. Easiest group to handle. Best prognosis.

Group 2.—32.3 per cent. of cases: Received in condition of moderate or severe acidosis (plasma bicarbonate  $\text{CO}_2$  below 40 volume per cent.), which clears up on fast.

Treatment: Made free of glycosuria and acidosis by continuous fast. A tendency toward acidosis is present.



and the safely tolerated maintenance diet is usually lower than on Group 1.

Group 3.—14.5 per cent. of cases: Tendency to slight acidosis (subnormal plasma bicarbonate) on any but most carefully chosen diet. Acidosis not increased by fasting.

Treatment: Glycosuria removed by continuous fast. Tolerated maintenance diet variable. Usually there is a tendency toward acidosis which may become acute on any improper diet.

Group 4.—6.4 per cent. of cases: Either develop or retain severe acidosis (plasma bicarbonate  $\text{CO}_2$  below 30 volume per cent.) when fasted to attain the aglycosuric state. This is incomparably more severe than the mild acidosis observed, as a rule, when normal individuals are fasted, and may rapidly become fatal unless the fall in plasma bicarbonate is checked.

Treatment: Continuous fast must be given up for intermittent fast. As in Group 2, the presence of a tendency toward acidosis is demonstrated and must be considered in future feeding and care of the patient.

On account of the clear manner in which the outline of this treatment is given and because of its great importance to practitioners, this abstract has been made long and inclusive, and contains extensive and direct quotations from the original article.

**Results in the Modern Treatment of Diabetes.** Results obtained in the modern treatment of diabetes at the Presbyterian Hospital in New York, are the basis of a paper by H. R. Geyelin.<sup>2</sup>

After four years or more of trial he considers it appropriate to review the therapeutic results that have been obtained with the Allen treatment for diabetes which has received such universal adoption by the medical profession. He laments the fact that while many practitioners who have employed the fasting treatment have quite generally appreciated the use of the preliminary fasting period to abolish glycosuria and acidosis, they have not fully appreciated the great importance of the subsequent method of regulating the diet and the importance of keeping the patient free from sugar and ketone bodies.

(2) Jour. Amer. Med. Ass'n, Oct. 18, 1919.

Probably the most important feature of the after fasting treatment is the proper regulation of the relative proportion in the amount of protein, carbohydrate and fat in the diet, and the appropriate distribution of half days and fast days.

The high fat feeding of former years is looked upon by Geyelin as having led to more fatal outcomes in diabetes than any other one factor. He is inclined to believe that coma may be averted in almost all diabetic patients, even in the presence of infection, provided the fat of the food is kept at the proper level or in extreme instances totally eliminated.

In order to demonstrate the favorable results of the modern treatment as carried out in the hospital named above, the author presents a table, whose figures indicate the results of the old and the new method of treatment.

#### RESULTS OF OLD AND NEW METHODS OF TREATMENT.

	Year	Cases			Deaths		Dish		Dish Ke-	
		No.	No.	%	No.	%	No.	%	No.	%
Old Method	1912	24	6	25.0	4	66.6	3	12.5	12	50.0
	1913	37	5	13.5	4	80.0	18	48.6	23	62.1
	1914	39	7	17.9	5	71.4	16	41.0	13	33.3
	1915	24	9	37.5	5	55.5	13	53.0	11	45.8
	Total	124	27	21.7	18	66.6	50	36.8	59	47.6
New Method	1915	19	1	5.0	0	0.0	16	93.5	14	73.6
	1916	71	8	11.2	2	25.0	58	81.6	57	81.0
	1917	90	11	12.0	3	27.2	78	86.4	60	66.6
	1918	95	12	12.6	3	25.0	82	88.1	70	73.0
	Total	275	32	11.6	8	25.0	234	85.0	207	75.3

From this table, it is evident that the number of patients treated by the modern method in 3½ years is more than double that treated by the old method over a similar period of time, the mortality percentage, however, is notably diminished. Under the new *régime* there were proportionately fewer deaths from coma, which is thought to be due to the early withdrawal of fat from the diet on admission to the hospital and the institution of fasting treatment. Formerly, that is up to 1915, from 80 to 90 per cent. of the patients who returned to the

dispensary for care after leaving the hospital were found to have traces of sugar or more than this amount in their urine, whereas under present day care, less than 40 per cent. returned for their regular visits showing sugar in the urine.

A further notable factor associated with the newer method of treatment is that in cases of gangrene, carbuncles and other local infections, the results of combined medical and surgical treatment, with its effect on the saving of life and the preservation of limb, have been very much better than with the previous method of treatment. In fact, many operative procedures which were done hitherto have been rendered unnecessary.

Geyelin points out that the most difficult part of the management comes after the original fast, which has been effective in eliminating glycosuria and controlling acidosis.

The next step is gradually to increase the food until traces of sugar appear in the urine. A fast, or half day, is then given to eliminate glycosuria and following this the patient is put on a slightly lower intake of carbohydrates, protein and fats, various ones of all these foods being gradually increased until a definite tolerance is determined.

In a general way the result desired is as follows:

A much higher allowance of carbohydrates than was customary under the older methods of treatment, an allowance of fat ranging from 130 to 180 gm. depending on the patient's tolerance (it may be much lower) and a protein intake of from 1.5 to 2 gm. per kilogram of body weight. The urine must be kept free from sugar and ketone bodies, while the blood carbonates and blood-sugar fasting value should be maintained at the normal or nearly normal level.

Half days or fast days, depending on the severity of the case, are given when sugar appears, and additional half days or fast days are given at regular intervals, with the purpose of increasing further tolerance. If with this system of treatment there is obtained faithful co-operation of the patient in following this diet and testing the urine daily, together with timely observations of the blood sugar, improvement unquestionably occurs for

periods of from one to three years at least, and possibly longer.

**Dietetic Treatment of Diabetes.** The dietetics of diabetes and glycosuria are discussed by W. L. Brown,<sup>3</sup> who says that the recent advance in the dietetic treatment of diabetes has been the result of convergence between three lines of research; the influence of proteins in exciting glycosuria, the value of green vegetables and egg diet, and the value of fasting.

The credit for formulating a systematic method based on these three principles belongs to Allen in America, and to Graham in England. They reached their conclusions independently almost simultaneously and by different routes. Allen's method was the result of prolonged experiments in such cases. Graham's was based on clinical observations.

Browne's impressions of the new treatment are summed up thus:

The actual fast, mitigated as it is by the taking of coffee, clear soup and lemonade, is usually quite well tolerated if the patient keeps at rest in bed. The days of meager diet, particularly that of green vegetable and egg, is more exacting. Appetite is excited and then inadequately satisfied. It is easier for these patients if they rest in bed until the total intake approaches 2,000 calories daily. Children seem to tolerate the treatment well. Graham's method, somewhat modified, is presented as follows:

Two hunger days: Tea and coffee as desired, and 500 c.c. of Bovril and broth, made without vegetables, divided into two equal portions. Water or lemonade, sweetened with saccharine, can be taken *ad lib.*

Followed by—

**Two Vegetable and Egg Days:**

**Breakfast:** Two scrambled eggs, with tea or coffee. 2 oz. (50 gs.) of lettuce, watercress, or tomato.

**Lunch:** 8 oz. Bovril or broth. One poached egg on spinach. Any green vegetables with  $1\frac{1}{2}$  oz. of butter. The total amount of the vegetables for the meal to be 6 to 8 oz.

---

(3) Practitioner, August, 1919.

*Tea:* Tea or coffee, lettuce, watercress, or tomato, 50 gs. or 2 oz.

*Dinner:* 8 oz. Bovril or broth. Two eggs, cooked as desired, *e.g.*, as savory omelette. From 6 to 8 oz. green vegetables with  $1\frac{1}{2}$  oz. of butter. Water or lemonade as desired.

This diet has a caloric value of 1,170 and a carbohydrate intake of about 10 grams.

*“Ladder Diet”:*

After two vegetable and egg days add 50 gms. of meat or 100 gms. of fish. This raises the caloric value to about 1,300. Two days later, add 50 gms. of bacon at breakfast and omit one egg. Add another 10 gms. of butter to the vegetables. The caloric value is now 1,595. Two days later, add 50 gms. of sardines at lunch, and omit one egg, or if the fish has previously been given, omit this and add 100 gms. of meat. The caloric value is now 1,635. Two days later, add 50 gms. of ham and omit another egg. The caloric value is now 1,795. The quantities of sardines and ham may be doubled if the patient is hungry, and the degree of acetonuria is slight. This brings the caloric value up to 2,145.

This diet is generally known as the “Ladder Diet,” and it will be noticed that it takes 12 days to reach the top of the ladder. If the patient is free from sugar when at the top of the ladder, add either 100 c.c. of milk (= 4 gs. carbohydrate) or 10 gms. of bread (= 6 gms. of carbohydrate in war bread, 5 gms. in ordinary bread). Increase by the same quantity every other day until the limit of carbohydrate tolerance is reached. If the patient is not sugar free when at the top of the ladder, repeat the whole process.

In general terms: The author gives two consecutive vegetable and egg days once a fortnight and two hunger days, followed by two vegetable and egg days, once a month, returning to the standard diet, as determined for the particular patient, immediately after these days. But the details of the after treatment must depend on the individual case. Rest in bed is advisable, at any rate till the caloric value of the food reaches 2,000.

**Treatment of Diabetes in Children and Adolescents.** While this article deals with the treatment of diabetes



mellitus in children and adolescents, there is much about it that will be beneficial to practitioners in general.

O. Leyton<sup>4</sup> states that diabetes in any patient can be determined safely only by finding out the quantity of carbohydrate, protein, and fat he is able to take without sugar or diacetic acid appearing in the urine, or perhaps more accurately without any excess of sugar appearing in the blood. (The normal quantity of sugar in the blood is 0.1 per cent. by Lewis and Benedict's method.)

When a diagnosis of diabetes mellitus has been made, a prognosis should not be given until observations have been made to determine how much of the various food stuffs the patient can utilize. It may be impossible to begin treatment immediately, and the question then arises as to the diet during the interval. An instrument may be used for the rapid estimation of the percentage of  $\text{CO}_2$  in the alveolar air, and this proves to be of the greatest value for if the amount is really low, that is, under 2 per cent., one must conclude that the acidosis is severe, and the patient must be ordered small quantities of carbohydrate and protein, but no fat whatever. Fat is the food which kills in circumstances of this kind. The examination of the patient should be systematic and complete. If any focus of infection can be found, it should be dealt with as expeditiously as possible.

The effect of any infection upon metabolism seems to be an unopened book. A small infection may lead to a great change in metabolism. This fact illustrates the importance of making every effort to free the patient from any infection before attempting to find the optimum diet. In removing an infection, local anesthesia and intraspinal anesthesia are permissible, but general anesthetics frequently lead to a great deterioration in metabolism which is not temporary but permanent.

When a patient is admitted to a hospital with a diagnosis of diabetes mellitus, he is put on a diet consisting of small quantities of carbohydrate and protein, with a minimum quantity of fat for two days. The quantity of protein must depend upon the weight of the patient rather than the age, while the quantity of carbohydrate depends upon the severity of the acidosis. A child weigh-

(4) Practitioner, November, 1919.

ing about 20 kilos, or 50 pounds, should receive 30 gms. of protein and between 10 and 30 gms. of carbohydrate. On this diet the acidosis will diminish rapidly and in the majority of cases, beef tea only may be given on the third day. The patient is not pressed to drink this tea, but may take as much as he likes, by having it slightly salted the quantity taken is increased, and this is to his advantage. Unless the child chooses to stay in bed, he is allowed to get up and go out; the more muscular exercise taken, the more rapid the disappearance of the sugar from the urine.

After the urine has been free from sugar for twenty-four hours, a small quantity of carbohydrate is given in the form of vegetable.

A diet table for a child weighing 20 kilograms, or 50 pounds, is presented, to cover a period of 16 days:

	Carbohy.	Protein	Fat	Calories
	gms.	gms.	gms.	gms.
1st day .....	2	0	0	8
2nd day .....	4	0	0	16
3rd day .....	6	6	5	93
4th day .....	8	6	5	101
5th day .....	10	12	10	178
6th day .....	12	12	10	186
7th day, beef tea.....	—	—	—	—
8th day .....	14	12	10	194
9th day .....	16	18	15	271
10th day .....	18	24	20	348
11th day .....	20	30	30	470
12th day .....	22	35	40	588
13th day .....	24	40	50	706
14th day .....	12	20	25	353
15th day .....	24	45	60	816
16th day .....	24	50	70	926

In order to maintain an individual at a constant weight it is necessary to supply 40 calories per kilogram body weight *per diem*; therefore, in order that a child weighing 20 kilos, or 50 pounds, shall maintain his weight, he needs a diet the energy value of which is 800 calories; 930 calories contain the necessary excess to permit growth.

One must consider what should be done if sugar returns before the sixteenth day is reached. If sugar re-

turns before the fifth day, it is fair to assume that the carbohydrate tolerance is so very small that it will be impossible to maintain the life of the child for any considerable time, and it would be wise to allow him to have the food he craves, and let coma, rather than inanition, lead to dissolution.

If sugar returns between the fifth and tenth day, it may be assumed that it is due to the increase of carbohydrate, and one should see whether by reducing the carbohydrate to 8 gms. *per diem*, a diet of protein and fat can be utilized without sugar returning. It is obvious that if the return of the sugar is due either to the protein or fat, life could not be maintained, and, therefore, keeping the carbohydrate at 8 gms., the protein is gradually increased, and the fat also, until the diet contains the necessary energy.

If sugar returns toward the sixteenth day, it may be due either to an excess of carbohydrate, an excess of protein, or an excess of fat. A day of alimentary rest should be instituted, and then the carbohydrate halved whilst the protein and fat are maintained.

If sugar returns on this diet, protein too must be halved. Should this lead to the continued disappearance of sugar, then the carbohydrate may be slightly increased, keeping the protein low. The condition is extremely serious, because a child taking less than 2 gms. of protein per kilo. daily is not likely to develop normally.

On the other hand, if it is found that fat is causing sugar in the urine, then it must be reduced and carbohydrate gradually increased until sugar returns.

The optimum diet is one containing two-thirds of the limit of carbohydrate tolerance, 2 grams of protein per kilogram weight and sufficient fat to make the energy of the diet equal to 60 calories per kilogram body weight.

The gradual addition of milk to a diet is not satisfactory, since it contains all three food-stuffs and prevents the optimum diet being found.

It is a great fallacy to believe that carbohydrate is responsible for sugar in all cases. The author has treated patients who were able to take a larger quantity of carbohydrates than of fat.

## DISEASES OF THE KIDNEY

**Chemistry of the Urine and Blood.** The facts presented in this discussion of chemistry of the blood and urine, by W. Boyd,<sup>5</sup> of the University of Manitoba, are not new. They are presented with such clearness, however, that even though they are well known to most physicians, it will be of value to have such a concise review of what is being done, what can be done in this field, and of the significance of the results obtained.

In the past, physicians have confined themselves largely to determining the waste products of the machine, often with no reference to the fuel which is being supplied at the same time. Such methods applied to the study of any delicate mechanism would be doomed to failure. It should be the aim to gain some idea of the morbid processes which are actually going on before any alteration in the nature of the waste products has had time to make its appearance. This is the aim of investigations into the chemistry of the blood, which are beginning to assume such an important place in modern medicine.

Most of the recent work that has been done in this field has had to do with the nitrogen metabolism and to recall some facts regarding the manner in which nitrogen is absorbed and disposed of by the body, is worth while.

The nitrogen of the food is contained in the protein molecules. The albumins and globulins of food proteins are disintegrated by the digestive juices of the stomach and pancreas into proteoses and peptones, and ultimately into amino-acids, of which there is a very large number, but all of which are distinguished by the possession of the group  $\text{NH}_2$ . The original protein molecule is a huge complex affair. The amino-acids of the protein molecule are crystalloid bodies of relatively simple constitution, easily soluble and readily absorbed. They have lost all protein characters.

(5) Canadian Med. Ass'n Jour., May, 1919.

When amino-acids pass through the intestinal mucosa into the portal circulation, some are carried through the liver and distributed through the body generally, where they combine with the tissues and are utilized partly for body building and partly for the production of energy. Others are decomposed by hydrolysis and undergo the process of de-aminization, in which the  $\text{NH}_2$  group is split off and converted into ammonia. This combines with the carbonic acid of the blood with the resulting formation of ammonium carbonate. Some of the  $\text{NH}_3$ , however, escapes this fate, and is used for neutralizing the acid bodies in the blood in combination with which it is excreted in the urine. If these acid bodies become increased in amount, less of the  $\text{NH}_3$  is available for conversion into urea, and more is excreted in the urine combined. It is thus evident that in the clinical condition of acidosis an increase of urinary ammonia will be a sign of great importance, which may make its appearance before the acid bodies can yet be detected in the urine. All the urea however, is not derived from amino-acids in the food. There is in the body a constant disintegration of the tissue protein, and the resulting amino-acids are carried to the liver, where they are converted into urea.

The nitrogen of the body occurs in two great forms: as protein nitrogen in albumin and globulin, with which this article is not specially concerned, and as non-protein nitrogen, the latter representing the simple disintegration products of metabolites of the former. The nitrogen partition, a term often used in modern literature on the subject, indicates the manner in which nitrogen is distributed among the various non-protein nitrogenous bodies. Of these, the most important are urea, ammonia, uric acid, creatin and creatinine. The last three are the more important of the purin bodies, which are derived from the decomposition of the nucleoprotein contained in the nuclei of the cells.

Uric acid has a double origin, partly exogenous from the nucleins in the foodstuffs, and partly endogenous from decomposition of the nucleins in the body tissues. Creatinine, derived from creatin in the tissues, is entirely endogenous in origin, being independent of food in-



gested, and thus affords an accurate and important index of the stage of nitrogen metabolism in the tissues.

TABLE ILLUSTRATING THE BEHAVIOR OF SOME CONSTITUENTS OF THE BLOOD IN UREMIA AND DIABETES.

Condition	Total N. P. N. Mgms. per 100 c.c.	Urea N Mgms. per 100 c.c.	Creatinine	Sugar Per cent.
Normal .....	25-35	12-20	1-2.5	0.08-0.12
Uremia .....	80-350	50-300	3-7	.....
Diabetes .....	.....	.....	.....	0.15-1.30

All of the above non-protein nitrogen substances are excreted in the urine, and their estimation either *in toto* or individually affords valuable evidence of conditions of disordered nitrogen metabolism. Still more important information is afforded by their estimation in the blood.

Examination of the urine from patients with nephritis must give information concerning albumin, total nitrogen and chlorides. The ability of the kidney to excrete urine is also indicated by the phenosulphonephthalein test. These tests should all be carried out with the patient on a standard diet of known constitution, such as that of Mosenthal, especially with regard to the amount of chlorides ingested. The normal response to such a test meal is 11 gms. of sodium chloride and 11 gms. of nitrogen. In parenchymatous or interstitial nephritis there is a marked drop in the chlorides which may amount only to 2 or even 1 gm., and a less marked drop in the total nitrogen, which, however, in advanced instances, may be 5 gms. or less.

It is pointed out, also, that one of the earliest evidences of impairment of function is a fixation of specific gravity, the variation falling to considerably below nine.

An increased excretion of urea occurs in fevers, owing to increased destruction of proteins, and a marked increase is seen during the absorption of an inflammatory exudate, and in the resolution stage of pneumonia. In these latter conditions there is a corresponding increase in the chlorides, for these salts are bound up in large quantities in the pneumonic exudates and in pleural and peritoneal effusions.

The urea is markedly diminished in diseases of the liver, especially in such conditions as acute degeneration. In these cases the ammonia excretion is high, for only a small amount of it is converted by the liver into urea. In nephritis there is a diminution in the urea, but only when the disease has reached a stage when it can be diagnosed by simpler methods. In such cases there is a corresponding increase in the blood urea.

Next to urea the most important non-protein nitrogen constituent of the blood is ammonia. The  $\text{NH}_3$  of the blood serves an extremely important function. It is one of the chief factors in keeping the reaction of the hydrogenion content of the blood at a constant level. When inorganic acids are ingested in the food, the  $\text{NH}_3$  in the blood combines with and neutralizes them, more  $\text{NH}_3$  appears in the urine, and less is converted into blood urea. Exactly the same thing happens when the organic acids in the blood reach a pathologic level, owing to the faulty metabolism of fats. In the acidosis of children, in the acidosis following surgical operations, and most of all in the acidosis of diabetes, the  $\text{NH}_3$  combines with the abnormal acids in an endeavor to preserve the alkalinity of the blood, and is therefore excreted in very large quantities in the urine. The important fact to be noted is that this increase often occurs a considerable time before the appearance of acetone bodies in the urine. In diseases of the liver, particularly in cirrhosis, there is often an increase of ammonia in the urine, owing to interference with the normal conversion of ammonia into urea by that organ.

The next subject considered is chemical analysis of the blood. Here the products of protein metabolism are represented by those substances included under the term non-protein nitrogen. The most important of these being urea, ammonia, uric acid and creatinine.

The normal figure for total non-protein nitrogen of the blood is from 25 to 30 mgms. per 100 c.c. In renal disease this becomes much increased and may rise as high as 350 mgms. per 100 c.c.

In chronic congestion of the kidney there is no retention, but in advanced nephritis the figure may be very high. Patients with over 100 mgms. usually die in four

or five weeks, even though the phthalein excretion may be fairly good. In uremia the non-protein nitrogen is always very high, but it is interesting to note that in eclampsia the rise is seldom marked. A marked elevation of non-protein nitrogen makes a patient a poor operative risk. Finally, Tileston and Comfort in a series of 142 cases found a considerable degree of retention in 36 per cent. of all syphilitics examined.

Urea constitutes 50 per cent. of the total non-protein nitrogen of the blood, and its estimation often affords information which throws a flood of light upon a case. When the urine urea of a patient is found to be very low this may be due to inadequate renal excretion, with blood urea above normal, or, on the other hand, there may be an insufficient formation of urea owing to some lesion of the liver, such as cirrhosis, carcinoma, acute yellow atrophy, or the lesions of eclampsia. In this case, the blood urea will be low, or at any rate not above the normal. This examination of the blood will explain the significance of the abnormal condition of the urine.

The estimation of blood urea is of great value in urologic surgery, not so much in diagnosis as an aid in prognosis, and in estimating the operative risk of a case. In kidney and prostatic cases if the blood urea is much above 100, the patient will most probably die shortly after operation from the development of uremia. An estimation of the variation in blood urea from week to week will afford valuable indication as to the prognosis in these surgical cases, a falling urea being a hopeful sign, a rising urea a bad one.

Creatinine constitutes only 2 per cent. of the total non-protein nitrogen of the blood, it is entirely endogenous in origin, and is thus a most important indication of the state of tissue metabolism. Of the three substances, urea, uric acid and creatinine, the last is the most easily excreted. Its retention is thus an indication that a most serious degree of renal inadequacy exists. The normal figures vary from 1 to 2.5 mgms. per 100 c.c. It may be said that a finding of over 5 mgms. indicates a fatal prognosis.

The metabolism of carbohydrates is next considered. Starch and the sugars that are more complex than glu-

cose are converted through glucose in the process of digestion and this substance is absorbed directly from the intestinal canal. The concentration of glucose in the blood is kept at a remarkably constant level—from 0.08 to 0.12 per cent. If the figure rises above 0.2 per cent. the kidneys are no longer able to hold it back, and it leaks through into the urine. The metabolism of the carbohydrates is dependent on and is regulated by the internal secretions of some of the ductless glands, chief among which is the pancreas. The pituitary, the thyroid, and the adrenals all, however, have an important relation to carbohydrate metabolism.

The amount of sugar which appears in the urine is by no means a certain indication of the condition of a diabetic, although of course a very valuable one. Not until the blood sugar has returned to normal limits can the patient's condition be regarded as satisfactory.

Boyd refers to the etiology of muscular dystrophy, concerning which there has been and remains much mystery. He says that evidence is now forthcoming which points to an involvement of one or more of the endocrine glands. Several cases have been recorded in which the blood sugar is well below the normal and the author reports a case under his own observation in which the blood sugar was remarkably low with a corresponding high sugar tolerance.

Closely related to disorders of carbohydrate metabolism is the subject of acidosis. In health the fats are burned up in the carbohydrate fire to non-toxic products. This combustion is complete so long as there is at least one molecule of carbohydrate to three of the higher fatty acids. In diabetes, this ratio cannot always be maintained, with the result that the fire begins to smoke with acid bodies from the incompletely burned fat. These acid bodies accumulate in the blood, and are neutralized by the bases of the blood, notably ammonia, as well as being taken up by the "buffer" action of such salts as di-sodium and mono-sodium-hydrogen-phosphate. The result of all this is to bring about an impoverishment of the bases of the body, and thus an inability on the part of the blood serum to combine with and eliminate the

acid  $\text{CO}_2$ . The clinical result is the appearance of the symptoms known as acidosis.

Acidosis may be recognized by the appearance in the urine of the acetone bodies, acetone, diacetic acid, and oxybutyric acid. Prior to this appearance, however, there is an increase in the combined ammonia of the urine, since the ammonia of the blood neutralizes the acid bodies to the best of its ability, and is excreted in increased amount. The acidosis may also be recognized by means of various tests applied to the blood of which the most valuable is the determination of the power of the blood serum to combine with and carry  $\text{CO}_2$ , a power which has invariably diminished in acidosis.

The presence of acetonuria must not, however, be regarded as certain evidence of acidosis, for acetone bodies may appear in the urine without any diminution in the  $\text{CO}_2$  carrying power of the blood. Further, there may be a true acidosis without any acetone bodies in the urine, as for instance in the retention of acid phosphates which often occurs in nephritis. When there is great disturbance of liver function, as in delayed chloroform poisoning and in the toxemias in pregnancy, there may be marked acidosis with large amounts of lactic acid and of ammonia in the urine, but with only a small amount of acetone bodies. Such cases are due to disturbance of nitrogen metabolism, rather than to that of carbohydrates.

The list of clinical conditions in which acidosis may play a more or less important part is being continually added to. The most important are diabetes, post-anesthetic conditions, starvation, infantile marmasmus, the cyclic vomiting of children, pregnancy, advanced nephritis, various febrile diseases, such as pneumonia, cholera, and conditions in which a deficiency in the oxygen-carrying power of the blood leads to asphyxia. It is a curious fact that a sojourn at high altitudes always produces a well-marked acidosis.

**The Clinical Significance of Blood in the Urine.** II. O. Mertz,<sup>6</sup> states first that one may consider any urinary hemorrhage an expression of a pathologic lesion located somewhere along the urinary tract. A survey of his own

(6) Jour. Indiana State Med. Ass'n, April, 1919.



work demonstrates the source of hemorrhage in the following order of frequency: kidney, prostate, bladder cavity and urethra. The most frequent cause was an inflammatory process; second, new growths, and third, various mechanical factors. Any combination of these processes may be found in one and the same case.

Of the kidney lesions, some form of nephritis has been the most frequent cause: pyelitis, or more frequently pyelonephritis and pyonephrosis, and intermittent hydronephrosis, a finding somewhat at variance with what has generally been accepted as true. Stone in the kidney, tuberculosis of the kidney, and neoplasm of the kidney occupy these relative positions in the patients studied by this author. He has found also that hemorrhage is not infrequently associated with benign hypertrophy of the prostate.

The bladder lesions encountered were cystitis, neoplasm and stone in the order in which these are given.

Inflammation of the urethra, especially when specific in type, may be accompanied by hemorrhage. External trauma, and the administration of certain drugs—cantharides, quinine, hexamethylenamine (urotropine), etc., may also produce hemorrhage.

Mertz considers that the information obtained by this review of his patients, covering a series of 100 cases of urinary hemorrhage, is probably a fair index of their occurrence in the average practitioner's hands. He emphasizes that the amount of bleeding and its type, whether intermittent or constant, does not indicate the severity of the existing lesions in the urinary tract. Also, he says that no reliance can be placed on the cessation of an acute hemorrhage as it is not unusual for this phenomenon to recur at varying intervals.

As routine measures in reaching a diagnosis in patients presenting this symptom, the author employs renal functional tests, makes repeated urine analyses, stains of sediment, etc., first, and in case the diagnosis is not made by these measures, he then performs cystoscopy and proceeds with the various other diagnostic measures, ureteral catheterization, radiography, pyelography, etc., as circumstances indicate.

He considers it unwise to begin the work by having *x-ray* pictures of the regions of the kidneys made.

Concerning hemorrhage from stone in the kidney he says that in every case in which stone in the kidney has come under observation and been recognized it has at some period of its development been associated with hematuria.

The most confusing and difficult case to diagnose that he has encountered was one in which the hemorrhage was due to a small papilloma of the urethra near the external urethral meatus.

While there are instances of urinary hemorrhage with symptoms that will enable one to make a diagnosis, there are many more in which special work is necessary in order to reach a definite diagnosis. In the care of such cases, at no time should one be satisfied until an accurate knowledge of existing pathology is obtained or until all available means of diagnosis are employed, and a physician does not dare under any other circumstances to assure a patient that everything possible is being done for him.

**Etiology and Cause of Hematuria.** With the modern methods of diagnosis, the origin and cause of hematuria can be obtained in the vast majority of cases.

Profuse painless hematuria may be and often is the initial symptom of nephritis, and these cases may have to be followed over long periods of time before a definite diagnosis of the nephritis can be made. Other cases in which no diagnosis, or only a tentative one is made, on further study will reveal the presence of tubercle bacilli.

From its site of origin, hematuria may be classified as coming from the kidneys, ureters, bladder and urethra.

Hematuria of renal origin may vary from a profuse hemorrhage to a few cells detected microscopically, and may persist for days, weeks or even months. It may be intermittent or continuous over a long period of time.

The cases of hematuria are divided by C. F. Young,<sup>7</sup> author of this article, into two main groups: first, those due to local causes, and second, those due to general conditions.

In the first group there are the following conditions:

---

(7) Jour. Kansas Med. Soc., April, 1919.

inflammations, thrombosis and embolisms, traumatisms, parasites, calculi, tuberculosis, tumors, both malignant and benign.

Under general conditions are included infectious diseases, such as typhoid, scarlet fever, malaria, yellow fever, pneumonia, etc., diseases of the blood, leukemia, hemophilia, scurvy and purpura, poisons and intoxication, such as cantharides, turpentine, quinine, etc., and pregnancy and lactation.

There remains a large group of cases that have heretofore been classified as essential hematuria. With increased information concerning the causes of hematuria, fewer cases are placed in this group. In many of the cases formerly classified as essential hematuria, the patients are now found to have glomerular nephritis, or papillary nevi. Many other causes are also reported. In almost all of these cases the hematuria is unilateral.

Considering hematuria due to pathologic conditions of the kidneys, renal calculus is mentioned first, and Young says it must be a very unusual case of stone in the kidney in which a positive or negative diagnosis can not be made. This is likewise true of stone in the ureter. Tuberculosis of the kidney is common. Kroenlin is quoted as stating that 30 per cent. of all surgical diseases of the kidney are tuberculous. This condition is usually unilateral in the beginning.

Tuberculosis of the kidney begins in the parenchyma and at operation, as well as at autopsy is not found involving the pelvis, ureter or bladder in cases in which the kidney is not involved also. In rare instances a slight trauma or prolonged irritation from a calculus may be the exciting cause of tuberculosis of the kidney.

In tumors of the kidney, hematuria is usually the first symptom noted in the adult. In such cases it is generally profuse, painless, and symptomless and not influenced by rest or exercise. The passage of clots through the ureter may cause renal colic. The hematuria may occur several years before any other symptom.

In children the condition is much more rare than in adults. Hematuria of ureteral origin is rare and is usually due to new growths or to stones. When of vesical origin it is only a sign of some disease. The general

causes here include the dyscrasias of purpura, hemophilia, scurvy, malaria, yellow fever, cholera, and the toxemias of chemicals, such as turpentine and cantharides. Local causes are circulatory disturbances, trauma, infections, and new growths.

Among the circulatory disturbances are varicosities of the mucous membrane, passive congestion, as in hepatic cirrhosis; the condition met with in obstructive prostatic hypertrophy of long standing in which all the urine is drawn off by a catheter at one time, thereby removing the counter-pressure, producing severe passive congestion of the whole of the urinary tract, causing hemorrhage, and often suppression of urine and death.

Trauma that frequently produces vesical hemorrhage is produced by rough catheterization, the presence of foreign bodies, including calculi, and external violence, as from kicks or falls producing contusions or ruptures.

Among the infections that produce hemorrhage from the bladder, tuberculosis stands first. The most severe degrees of vesical hemorrhages are caused by tumors. Papilloma and carcinoma are of first importance. Vascularity is the main feature of these growths, and the friability of the structures leads to the breaking down of the hemorrhage. The diagnosis is made more easily in these cases by the cystoscope. If seen early, practically all the villous papillomata respond readily to fulguration but, unfortunately, malignant papillomata and carcinoma do not respond well to this method alone.

Bladder stones produce hematuria in the vast majority of instances, although the bladder may be absolutely packed full with one large stone, the patient apparently is not uncomfortable and notices nothing wrong with the urine. Diagnosis in these cases is made by the cystoscope and the *x*-ray.

Hematuria of urethral origin may be due to the following conditions: papillomata, prostatic hypertrophy in old men; simple ulcers; strictures; verumontanitis; bleeding from varicose veins and bleeding from mucous membranes that show no pathologic lesions.

The author presents the following summary:

The three most frequent causes of profuse hematuria are tumor, stone, and tuberculosis.

Hematuria being a frequent symptom of tumor formation in the urinary tract, this should be considered in every case of painless, profuse hemorrhage until the possibility is excluded.

The use of the term "essential hematuria" should be discouraged, and the real cause of the hemorrhage searched for.

Each patient suffering with hematuria should be impressed with the seriousness of the condition and the necessity of determining the exact cause where possible.

**Renal Function Influenced by Intestinal Obstruction.** The literature on the intoxication of intestinal obstruction reveals the fact that no direct study has been made of the renal function in this condition. Yet, there is indirect evidence of functional impairment in spite of the fact that the present histological methods fail to show definite alterations of the kidney parenchyma.

These statements are made by Irving McQuarrie and G. H. Whipple<sup>8</sup> of the Hooper Foundation, University of California Medical School, as an introduction to their article dealing with the influence of intestinal obstruction upon renal function.

After a brief review of literature upon this subject they present the method by which they studied the problems.

Dogs, mostly females, were used in all the experiments. Only healthy young adult animals were selected after being under careful observation for several days at least, during which time the urine was examined with reference to its specific gravity, reaction, and albumin and cast contents. After the animals had been thus observed for a period of from three to five days, a simple obstruction of the small intestine was made by section of the intestine with inversion of the cut ends. In one dog an isolated loop of ileum was made and the remaining ends of the intestine were united by a lateral anastomosis.

Three methods for the measurement of renal efficiency were used. First, that of measuring the urea-excreting capacity of the kidneys; second, the phenosulphonephthalein elimination method of Rowntree and Geraghty;

(8) Jour. Exp. Med., April, 1919.



and third, that of determining the rate of excretion of injected sodium chloride.

The first method, that of measuring the power of the kidneys to excrete urea, was carried out by determining the blood urea and simultaneously the rate of urea excretion, in most instances after the injection of urea. These values were expressed in the form of the following ratio:

Urea in 1 hour's urine

---

Urea in 100 c.c. of blood

The protocols of a number of the experimental animals are presented with tabulated results, which show that undoubtedly the excretory functions of the kidneys is decidedly impaired in this condition. Individuals with intestinal obstruction show a heaping up of all non-protein nitrogenous substances in the blood. Urea is most conspicuous in this material. The kidney is evidently unable to secrete any of these nitrogenous substances with its normal facilities. These substances are being formed with abnormal speed, so that there is a great accumulation in the blood and tissues. The kidney in this condition reacts like the kidney of chronic nephritis, although there is no anatomic injury, and the kidney of intestinal obstruction is only temporarily insufficient. With relief of the obstruction and clinical recovery the kidney function returns to normal. This injury can be repaired easily and leaves no trace behind, in so far as modern histologic methods can show.

The authors point out three important facts concerning the intoxication of intestinal obstruction:

1. There is a great increase in the elimination of urinary nitrogen which is dependent on the intoxication.

2. There is a great increase in the non-protein elements of the blood. These two facts indicate cell injury.

3. There is a decrease in kidney excretory function which is most clearly shown by the inability of the kidney to secrete the normal amounts of urea, sodium chloride and phenolsulphonephthalein.

The authors believe in picturing this reaction in the kidneys as a part of the general cell protein injury which results from the presence of the obstructed intestine.

The poison, they say, acts directly upon the epithelium of the kidney and causes temporary paralysis or impairment of its secretory function. There is no histologic evidence of any cell injury, but they realize that function may be impaired without any definite change in structure. Repair of this injury may be effected in from twenty-four to forty-eight hours after clinical recovery from the intoxication.

They state that in the treatment of this condition no physician can afford to ignore the established fact that a definite impairment of the kidney functions develops as a part of the intoxication of intestinal obstruction. The two conditions usually parallel each other closely. The degree of intoxication which may develop in ileus is sometimes hard to evaluate clinically. They suggest that the non-protein nitrogen or urea-nitrogen of the blood, as well as the renal function, may give warning of a grave intoxication which may be masked clinically. The ileus may persist with stormy symptoms for many days without grave intoxication. Again, the condition may appear to be mild clinically yet associated with high blood urea and a low renal function. In the last instance there should be no doubt of a serious intoxication and the necessity of urgent measures.

A continuation of the above work, and by the same authors<sup>9</sup> is carried out in a somewhat modified manner. They consider it established that the intravenous injection of the toxic proteose material isolated from the content of the obstructed small intestines produces symptoms closely resembling, if not identical with, those characterizing the intoxication of acute ileus. It was decided, therefore, to employ this more simple method of inducing intoxication for a supplementary study of the renal function.

For this purpose young dogs were studied in a preliminary period as described in the above article. After such a preliminary study the dog was given a dose of the toxic material isolated from the content of an obstructed intestine. From one to three hours after this injection the different renal function tests were applied as in the control period.

(9) Jour. Exp. Med., April, 1919.

The process of isolating the poisonous materials in loops of dog's intestines that had been acutely obstructed and from human bowel obtained at autopsy, is described in detail.

In summarizing the results obtained, the authors say that the injection of the toxic proteose obtained from the contents of the obstructed small intestine causes definite impairment of the eliminative function of the kidneys, as shown by a decreased capacity to excrete urea, sodium chloride, and phenolsulphonephthalein. This involvement of the renal function is similar to that shown by the preceding report to accompany the intoxication of intestinal obstruction.

The observed depression of function is readily demonstrable, even when large amounts of fluid and urea, dye, or salt are injected directly into the blood-stream. There is in all probability a temporary injury of the kidney cells, since the most important extra-renal factors have been largely eliminated, by previous work. There is no appreciable impairment of the renal function following the injection of a number of other proteose preparations.

This study affords new evidence in favor of the view that the function of an organ can be profoundly disturbed for a time without any demonstrable anatomic lesions. The repair of this type of injury promptly follows the disappearance of the intoxication and is functionally and anatomically perfect.

**Blood Plasma Chlorides and Renal Function.** A study of blood chlorides, blood urea-nitrogen, and the ability of the kidney to excrete phthalein, has been carried out by W. C. Rappley,<sup>1</sup> of San Francisco, former pathologist to Foxborough State Hospital, in Massachusetts.

The subjects used for this study were inmates of the institution at Foxborough, and all were workers in the industrial rooms, wards, or on the farm. None of them showed any edema, cyanosis, dyspnea, or other features which are known to compromise excretory rates.

An introductory statement is to the effect that the significance of the chloride content of blood is imperfectly understood. Special information in relation to the prob-

(1) Boston Med. and Surg. Jour., Jan. 22, 1920.

lem has been summarized by McLean, who is quoted as follows:

The normal and usual range of concentration of blood plasma chloride is from 562 to 625 mgm. per 100 c.c. of plasma or higher, according to the amount ingested. On the excess over 562 mgm. per 100 c.c. of plasma depends the rate of excretion.

There is a relative increased concentration in certain cardiac and renal diseases.

Under certain conditions, notably fevers and diabetes, or by the action of diuretics or heart tonics, the chloride threshold may be temporarily or permanently lowered.

Failure to excrete chlorides in pneumonia is associated with a lowered concentration of chlorides in the plasma.

Edema is usually accompanied by a relatively increased concentration of chlorides in the plasma.

Chlorides and urea functions are quite independent of each other.

During the work that constitutes the basis of this article, studies on renal function consisted of determination of the plasma chloride values, and a comparison with the elimination of phenolsulphonephthalein, the blood-urea findings, blood-pressure readings, and the specific gravity of the urine. Other features of the urine analysis were disregarded. The ages of the patients varied from 40 to 85 years, and the majority were over 50. None was taking drugs of any kind. The blood in every instance was drawn before breakfast, some twelve hours after the preceding meal. One hundred and four patients were studied in this manner. The results obtained are tabulated, and from them the author says that one is not permitted to draw a conclusion that the plasma chloride figures bear any relationship to the other features taken as evidence of renal functions.

A second group of forty subjects was studied and the plasma chlorides of blood found twelve hours after the preceding meal were determined and compared with figures determined from three to four hours after a regular meal. The values so found are tabulated, together with the blood urea-nitrogen, the phenolsulphonephthalein output, blood-pressure and urine specific gravity. Eighty-five per cent. of the men showed a defi-

nite rise in plasma chlorides after the meal, but an attempt to correlate the rise with any feature of the renal function as evidenced by the other findings enumerated fails. In both series there was little tendency toward a low fixation of the specific gravity of the urine.

Attention was later turned to the so-called cases of essential vascular hypertension, as seen in out-patient clinics and wards of a general hospital. These patients showed no evidence of nitrogen retention or depressed phenosulphonephthalein output to suggest that the origin of the hypertension was failing excretory function.

**Renal Glycosuria.** This study of renal glycosuria by Frederick M. Allen, M. B. Wishart and L. M. Smith,<sup>2</sup> was carried out at U. S. Army General Hospital Number 9, where of forty cases of supposed diabetes, three were found that belonged to the class of so-called renal glycosuria.

While it was not possible under the circumstances to carry out comprehensive research on these patients, a careful study of diet, of general metabolism, and relation of sugar content of blood to urine, of volume of blood, and volume of urine, was made.

The observation of three cases, as compared with thirty-seven cases of true diabetes in military service, and the increasing number of reports in the literature as blood sugar analyses are more employed, indicate that "renal" glycosuria is not so rare as once supposed, and probably is much commoner than other anomalies such as pentosuria or levulosuria.

The etiology, whether congenital or acquired, is unknown in two of these three cases. The history in one case is of special interest, as suggesting that severe trauma was either the primary or the exciting cause.

There was no indication of nephritis or renal abnormality in any of the three cases, except a slightly subnormal phenolsulphonephthalein elimination.

The apparent absence of harm in all three patients on unrestricted diet with continuous sugar excretion agrees with the favorable prognosis of this condition according to the literature. The only disturbance of health is that resulting from the severe restrictions of diet neces-

(2) Archiv. Int. Med., Nov. 15, 1919.



sitated by an attempt to stop the sugar excretion. The sharp contrast with true diabetes in this respect is of theoretical as well as practical interest.

No fixed relations were observed between the sugar in blood and urine. The renal excretion does not necessarily serve to maintain a low level of blood sugar. The output is not always higher with high than with low blood sugar.

No fixed relations were observed between sugar and water elimination, in the sense either of polyuria due to glycosuria, or a flushing out of extra sugar by increased diuresis.

The sugar excretion seems to be determined by the supply of available carbohydrate, especially preformed, but also to less degree by the potential carbohydrate of protein. The fat ration and total metabolism, which are important in true diabetes, are probably without influence here.

Analyses of blood fat in one case showed abnormalities from which no conclusion can be drawn. No abnormal tendency to acidosis was observable in any of the three cases.

The excreted substances in one of the three cases seemed to be an unknown sugar, distinguished from glucose by the absence or incompleteness of fermentation. This may be the most important observation of the present study, and suggests the desirability of closer examination of the fresh urine in such cases for accurate identification of the sugar.

The nature of so-called renal glycosuria is not established. Frank's hypothesis of a high plasma sugar did not hold in these three cases. It is not yet proved that the abnormality lies in the kidney, or that it consists merely in a lowering of the normal threshold of sugar excretion. It is possible that cases differ in kind as well as degree, and that a group of anomalies have heretofore been included under this name.

**A Study of Renal Infections.** In a previous publication by R. D. Herrold and H. Culver,<sup>3</sup> a report on the bacteria found in pyogenic renal infections was made in which it was stated that 8 per cent. of 116 patients were

infected with Gram-negative colon-like organisms either in pure or mixed form. No attempt was made at that time to classify these organisms other than to determine that they belonged to the colon or closely allied groups.

Clinical observations indicate that there must be either a vast difference in the virulence of the various strains in the colon group, or an equally marked difference in the susceptibility of individual patients. The contrast in the lesions produced and course of the infection between the staphylococcus infections and those of the colon group as a whole is well known. It may be that equally prominent and important differences exist between the infections produced by the various colon groups.

The purpose of the present paper is a classification of eighty-six different strains of colon-bacillus-like organisms by means of cultural, fermentative and serologic methods. These organisms were all secured by ureteral catheter from the kidneys and isolated by cultivation on blood-agar plates.

The conclusions reached by this study were as follows:

In a series of eighty-six strains of Gram-negative bacilli from renal infections but one-half were found to be true colon bacilli, the other half being paracolon organisms.

The true colon bacilli were found, by means of fermentative reactions, to be members of four distinct groups. This grouping bears no relation to specific antibody reaction, since an antiserum for any one organism does not react with equal vigor against other members of the same or different groups.

By means of agglutination tests, it was demonstrated that the colon group is markedly heterogeneous, as a monovalent serum reacts almost specifically. The paracolon group, however, while more closely related serologically than the members of the colon group, is still a heterogeneous group, but many members of this group reacted exactly alike in every respect.

There is no apparent clinical similarity between any two infections by members of any group or subgroup. The difference between the various infections seems to

be due to local or general conditions of the patient and not to any particular Gram-negative bacillus.

**Hematogenous Infections of the Kidney.** In beginning this discussion, W. J. Mayo,<sup>4</sup> refers to the work of Richard Bright, who in 1827 and 1836, pointed out that fundamentally there are two kinds of nephritis: Type 1, the "acute" or "wet" nephritis; and Type 2, the chronic or "dry" nephritis.

The first of these types, as understood today, is usually the result of toxins developed in the course of infectious diseases, as diphtheria, scarlet fever, tonsilitis, etc. In adults, exposure to colds, especially of the cutaneous surface of the body, plays a definite rôle in producing this type. It may be produced also by toxic agents, such as cantharides. The edema in such nephritis is to a large extent due to a failure of elimination of chloride.

Type 2, called by Bright "dry" nephritis, because edema is not present, involves the connective tissue and blood-vessels, especially the arteries. The patient suffers from headaches, nausea, vomiting, hypertension and other symptoms of uremia. Changes in the heart are so characteristic of chronic Bright's disease that the appellation of cardiorenal disease is at times not inappropriate.

A third type of nephritis, which is now brought forth, is one that results from living organisms. True nephritis is concerned with the filter portion of the kidney, and the failure to filter out all the bacteria and their retention is responsible for the occurrence of one form of the disease, which is of great surgical importance.

As to just how often such infections may be ascending or lymphogenous rather than hematogenous in origin, there is a diversity of opinion. Mayo believes that such infections, other than hematogenous, are extremely rare, so far as the kidney filter is concerned, so it is possible that they may be more frequent in that part of the kidney devoted to collecting urine.

It is evident that the effect of organisms on the kidney will depend on the nature of the bacteria, their number and on the condition of the kidney itself, on whether, for example, there is an anomaly present, such as hy-

(4) Jour. Amer. Med. Ass'n, Oct. 4, 1919.

dronephrosis or calculi, which makes the kidney more vulnerable. Also, when nephritis is the result of living bacteria the kidneys may be involved unequally, or unilaterally the unilateral infection being in the kidney which is more vulnerable, because of some physical defect.

Hematogenous nephritis is often caused by cocci found in the skin, especially staphylococci derived from boils, carbuncles, etc., and from focal infections generally. The staphylococcus is short lived and often affects only one kidney. Acute streptococcus infections are most malignant. Sub-acute and chronic streptococcus infections occur commonly as the effect of septic endocarditis, and appear in the kidney as a terminal infection, embolic in character.

Mayo emphasizes the fact that nephritis has been studied largely from a clinical and a necropsy standpoint. The surgeon, by opportunity, furnishes the missing link in these investigations, which carries the truth, and makes possible an exact study of the kidney before the terminal infections which are encountered at necropsy obscure the picture.

Payne and McNider and Buerger are quoted as having shown the hematogenous origin of certain of the so-called chronic, essential hematurias, demonstrating that infection in and about the straight tubules, resulting in the development of scar tissue which interferes with the venous circulation, causes congestion and varicosity of papillae and leads to rupture and renal hemorrhage. This gives a pathologic explanation for several cases in which formerly explorations were made to find the cause of renal hemorrhage, and in which one or more papillae were found to be the seat of varicosity.

In a number of instances of the chronic form of hematogenous nephritis of bacterial origin, the author has explored and found small cortical pimple-like collections of fluid in the kidney in various stages of sterilization. He has also encountered occasional deposits of calcium carbonates in such an infected area. The patients in whom such findings were made usually complained of pains that are now believed to have been caused by the kidney conditions just mentioned.

It is also evident, Mayo says, that in some painful kidneys, with dense scars in the capsule, the origin is similar and the condition may be relieved by decapsulation. It is admitted that capsular compression of the kidney could be the cause of symptoms, and the author relates having seen at least three cases in which hypertrophy of the remaining kidney within its fibrous capsule after the removal of its fellow for disease produced pain from the stretching of the capsule. He believes from his experience that the decapsulation has been valuable in this small group of cases in which there are scars and lime deposits in the capsule of the kidney, and in another group, still more rare, that of acute nephritis, in which the operation occasionally enables the kidneys to functionate when urinary function has ceased, and the patients are apparently in a dying condition.

**Diagnosis of Renal Colic.** The most common causes of renal colic, according to G. W. Stark,<sup>5</sup> of Syracuse, New York, are as follows: Strictures of the ureters, kinks in the ureters, stones obstructing the ureters, tying off of the ureters, and pressure from without, such as tumors. Occasionally the ureter may be caught by an adhesion external to the ureter.

Among the symptoms frequently encountered in this condition are anorexia, dyspepsia, nausea, flatulence and constipation. These gastric symptoms come and go with the colic pain. Nervousness, irritability, symptoms of hysteria or neurasthenia are concomitant with renal colic.

The diseased conditions that are easily confused with renal colic in making a diagnosis, are appendicitis, diseased adnexa, gall-bladder disease, duodenal ulcer, peritoneal adhesions, neurasthenia, pancreatic disease and lumbago. In appendicitis, the rigidity and leukocytosis are more marked. Elimination of gall-bladder disease, jaundice, turbid bile in Einhorn's bucket; duodenal ulcer, blood on string or blood in Einhorn's bucket, and *x-ray*; and pelvic examination to eliminate pelvic disease should help to clear up the diagnosis.

Any patient with pain in either side, who shows pus in the urine, or frequency of urination, or in some course

(5) New York State Jour. Med., September, 1919.



of the disease a history of a typical attack should be investigated by a urologist.

The most common type of the pain in this condition is that which begins in the loin and radiates downward along the course of the ureter toward the bladder, to the ilium, sometimes to the leg, and at times to the ovary or testicle.

Whether an obscure pain in the abdomen or back is caused by an obstruction in the ureter or other pathology in the abdomen can be very accurately diagnosed by means of the cystoscope, ureteral catheter, by pyelography, x-ray and functional tests.

The treatment in cases of stricture or kink in the ureter is as follows: The ureter is dilated from two to four points at intervals of from five to fifteen days. Following the dilatation, the pelvis of the kidney and ureter are instilled. Having first determined the size of the kidney pelvis with boric acid solution, the pelvis of the kidney is injected with about two-thirds of the amount of a 25 per cent. solution of argyrol. If the argyrol fails to clear up the infection of the kidneys, full dilatation of the ureter is accomplished, using a No. 8 ureter catheter and a 1 to 4 per cent. solution of silver nitrate is injected into the pelvis of the kidney, the amount used being two-thirds the normal capacity. The catheter is left *in situ* until the silver nitrate drains out. When the infection of the pelvis of the kidney is most prominent, the kidney lavage with argyrol is repeated as often as every other day, but when the obstruction is more prominent the treatment is less often given, usually every one to ten days.

It is the opinion of the author that if this method of treatment be used in most cases of pyelitis in which the infection has not extended into the substance of the kidney, the patients will recover.

Strictures can be remedied and ptosis of the kidney with kinks in the ureter can systematically be cured by the same treatment, plus a belt, and the results are uniformly more successful than those obtained by surgery, although the dilatation may have to be repeated.

The author has treated 146 cases of renal and uretral disease, making over 1,000 kidney lavages. He has never

seen any bad results from the above treatment. Of the 146 cases, six were essential hematuria and were cured by lavage of the kidney pelvis. Of twenty-one cases of kidney ptosis treated, nineteen were systematically cured. Eight patients had stone in the kidney, in five of whom it was successfully removed surgically: two nephrectomies were performed, one patient refused operation and lives still. Three had stone in the ureter, two were successfully advanced down the ureter into the bladder by dilatation. The other must be removed surgically. Eighty-four were pus kidneys, with or without obstruction. In twelve cases it was found necessary to do a nephrectomy: sixty-nine patients have been cured of pus in the kidney by means of lavage of the kidney pelvis and dilatation of the ureter.

**Importance of Early Diagnosis of Unilateral Renal Tuberculosis.** While this article deals with the surgical treatment of unilateral renal tuberculosis, the importance of early diagnosis of the condition is also greatly emphasized and places it easily in the realm of literature that interests the internist and general practitioner primarily.

At the outset, H. L. Kretschmer,<sup>6</sup> of Chicago, states that there are still many physicians who are unaware of the fact that the best form of treatment for renal tuberculosis is surgery. While under certain circumstances one may resort to the use of tuberculin, fresh air, hygiene, etc., in order to fortify the patient before operation, this must not be construed as meaning exclusively medical treatment.

Bearing on the diagnosis, he urges that if the general practitioner will keep in mind the possibility of tuberculosis in each case of cystitis that does not yield within a reasonable time to the usual treatment, many more early diagnoses would be made, and hence an increasing percentage of better end-results would be obtained.

In this field of medicine various diagnoses other than the correct one are abundant, many of the patients having been operated upon for disease of the pelvic organs or the appendix, without obtaining any relief or cure of the symptoms. Frequency of urination, associated with

(6) New York State Jour. Med., April, 1919.

other evidence of tuberculosis, should immediately arouse suspicion that a case of urinary or genital tuberculosis is being dealt with. Any evidence of glandular tuberculosis, either active or healed, should immediately be sought for, and should at once, if found, point out the way for a study of the gross clinical evidence which is easily obtainable.

The next step is the demonstration of tubercle bacilli in the urine, and their presence calls for further study in order to discover the location of the tuberculous process.

While the demonstration of tubercle bacilli in the urine is generally looked upon as being a most difficult and frequently an impossible task, the author insists that it is usually not difficult and is, indeed, far from being impossible in most instances.

In case tubercle bacilli can not be demonstrated in the urine, and the clinical symptoms and signs lead to a diagnosis of tuberculosis, one may then resort to the use of the guinea-pig. The injection of the animals with urine from a patient who has tuberculosis of the genito-urinary tract leads, in a high percentage of cases, to a definite diagnosis, because the animal develops tuberculosis, but even this method fails in some instances.

Having carried out these methods in obtaining all the information possible in this way, the cystoscope and ureteral catheter are next resorted to for demonstrating the origin of pus and tubercle bacilli from one side and the presence of clear urine from the opposite side, thereby establishing the diagnosis.

One of the great difficulties in making a diagnosis of unilateral tuberculosis of the kidney is presented by the instances of closed tuberculous pyonephrosis, where pus and tubercle bacilli do not reach the bladder.

Another great difficulty is encountered in the group of patients in whom both pus and tubercle bacilli may be demonstrated in the urine, and because of a contracted bladder cystoscopic examination can not be carried out.

In instances in which the author suspects tuberculosis, but can not demonstrate the bacilli, he uses an operating

cystoscope and excises some of the edematous mucous membrane and subjects this tissue to histologic diagnosis.

In the small group of cases in which cystoscopy can not be carried out, the Roentgen ray is a valuable agent in establishing the diagnosis.

Exploratory operation for establishing such a diagnosis is **very rare**.

Concerning tubercle bacilli in the urine, it is pointed out that a patient may be suffering from well-advanced tuberculosis of the kidney, and yet the urine may be free from pus. This may occur in cases in which the ureter of this side is completely occluded, and hence, the pus and bacilli will not be passed in the urine. This is mentioned to emphasize the possibility of the patient having an advanced renal tuberculosis, and yet at the time he presents himself for examination, the urine may be clear and free from pus.

Another serious and important problem that is often difficult to interpret is the presence of the tubercle bacilli in the opposite but supposedly well kidney. Possible sources of error that have been pointed out here are, according to Beer, first, an excretory phenomenon; second, the result of a reflux up the ureter of bladder fluid containing bacilli; and third, gross contamination from cystoscope or ureteral catheters despite the greatest care.

Under the heading of treatment, the author refers first to medical care of such patients. Whatever form of treatment or management leads to the disappearance of tubercle bacilli from the urine, so that they can not be demonstrated by injecting the urine into guinea-pigs, must be assumed as being sufficient to cure the patient. The diminution, or even complete disappearance of pus from the urine, however, may be only a transitory condition, likewise the diminution or disappearance of the bladder symptoms may be a temporary condition.

Dependence on general measures of treatment is dangerous on account of the constant tendency to a progressive destruction of the kidney tissue and a descending infection.

From such consideration, one is led to the statement that the treatment must be surgical in all cases of uni-

lateral renal tuberculosis, and the earlier the treatment is executed the better for the patient, provided, of course, that the second kidney is present and its function has been established.

The average mortality rate for nephrectomy for renal tuberculosis has been variously stated as from 2 to 4 per cent. This will depend on many factors. In order to give the patient the best end-result, namely, complete relief of the bladder distress, the diagnosis must be made early and operation performed as soon as the diagnosis is made.

**Effect of Foreign Protein on Kidney.** The purpose of this investigation by E. T. Bell and T. B. Hartzell,<sup>7</sup> was to determine whether chronic nephritis can be produced experimentally in rabbits by a foreign protein. Repeated shock was produced in a few animals, but in most of the experiments no attempt was made to produce anaphylaxis.

Special effort was made to eliminate various sources of error in the work. For instance, animals that had no signs of nephritis were carefully selected. Detailed protocols of the experiments carried out are presented in the original article. The authors state that these experiments indicate that ascitic fluid does not injure the kidney of a rabbit when injected intravenously in moderate amounts. The occasional small foci of lymphocytes found at necropsy in the injected animals can hardly be attributed to the protein, since such lesions are commonly found in non-experimental animals and were not excluded by the preliminary examination. Lesions of this size produce no changes on the kidney surface and seldom cause albuminuria.

The production of anaphylactic symptoms repeatedly did not cause nephritis. The symptoms were usually rather mild, but it is not possible to produce severe shock repeatedly. The animals either die or become refractory. The symptoms were apparently nearly as pronounced as in the experiments of Longcope and Boughton.

Egg-albumin in large doses seemed to cause a mild parenchymal injury of the kidney occasionally, but no



chronic changes of any kind were produced. This protein seems to be only mildly toxic for rabbits.

Sheep serum, however, is evidently toxic for rabbits, especially in relatively large doses. Several animals died shortly after a single injection. It produces a tubular injury to the kidney, but this is not severe enough to cause the death of the animal. There is no evidence of special glomerular injury. Degenerative changes only were observed in the first three experiments; but during the summer inflammatory renal lesions were found in four rabbits. This is evidently the same lesion which Longcope obtained. It undoubtedly developed during the course of the experiments, since it was not present at the beginning. It is similar in all respects to ordinary spontaneous nephritis. Like the spontaneous disease it would seem to be due to a bacterial infection, since pure cultures of streptococci were obtained from the kidneys of two rabbits.

Concerning the etiology of human chronic nephritis the authors share the view now widely held that streptococci are the main causative agents and that they first produce acute glomerular lesions which in many instances heal, but in others pass into a chronic stage. The continuous escape of streptococci from the focal infections through a diseased mucus membrane would theoretically favor the development of chronic glomerular lesions. However, so far, no one has been able to furnish experimental proof to support this theory.

The following summary is presented:

Non-toxic foreign protein, such as ascitic fluid, does not produce renal injury of any kind in the rabbit when injected intravenously in moderate amounts. The repeated production of anaphylactic symptoms with this protein likewise does not injure the kidney.

Egg-albumin may produce slight parenchymal injury when injected in large amounts, but usually it causes no damage.

Toxic foreign proteins such as sheep serum produce considerable parenchymal injury to the kidney which in some instances seems to lead to the rapid development of a renal infection comparable in all anatomic respects to the ordinary type of spontaneous nephritis.

The fact that streptococci were isolated in pure culture from the kidneys of such animals shows that the lesion is essentially infective, and not the direct result of foreign protein or anaphylotoxin.

No lesion comparable to human chronic glomerulonephritis has been produced experimentally.

There is no experimental evidence that foreign protein is in any way responsible for chronic nephritis in man.

### **Uric Acid in Early Chronic Interstitial Nephritis.**

A preliminary paper dealing with a study of the renal concentration power for uric acid in early chronic interstitial nephritis is presented by R. Upham and H. A. Higley.<sup>8</sup>

Their work comprises a study of the renal concentrating power for uric acid in early chronic interstitial nephritis, in the non-nephritic kidney, and in cases showing indefinite clinical or urinary symptoms, in which a diagnosis of nephritis was not possible by present methods.

The patients observed were placed on a specified diet and fluid intake for forty-eight hours previous to taking the blood and urine specimens. These were taken simultaneously between 11 and 12 a. m. In the original article the entire specified diet is given in detail. Its total caloric value was 2,880 calories a day. Three milligrams per 100 c.c. was accepted as the high normal limit of blood uric acid. High figures for blood uric acid were obtained in 85.6 per cent. of the patients with nephritis. On the other hand 40 per cent. of the patients who did not have nephritis also gave high figures for blood uric acid. This is taken to indicate that while high blood uric acid is an exceedingly common symptom of early chronic interstitial nephritis, it is by no means a specific one. Its availability for the early diagnosis of that disease is therefore materially limited. It was also noted that in early chronic interstitial nephritis the height of blood uric acid increase is not a guide to the degree of impairment of the renal concentration power. There is no direct relation between the amounts of blood uric acid and the concentration figure. The concentration figure

(8) *Archiv. Int. Med.*, November, 1919.

is obtained by dividing the blood uric acid content by the urine acid content. In early chronic interstitial nephritis the degree of impairment of the renal concentration function is not accurately gauged by mere blood uric acid content.

In the non-nephritic it would seem that as the blood uric acid content rises the renal concentration power falls, and as the blood uric acid content falls, the renal concentration power rises. For a perspective of the concentration figures observed in this work, the patients are considered in their clinical groups as follows:

First, a group (No. 1) which shows clinical symptoms diagnostic of nephritis. These all show a concentration figure of 14 or below.

Second, a group (No. 2) which shows no clinical symptoms suggestive or diagnostic of nephritis. These all show a concentration figure of 20 or above. The divergence in concentration figures between these two groups is definite and marked. Such figures give a clean-cut division which leaves no room for doubt. No such clean-cut division is afforded by the blood uric acid content.

Third, a group (No. 3) which shows clinical symptoms suggestive but not diagnostic of nephritis. These all show concentration figures below 18.4.

It is the belief of the authors that this group in reality belongs with the positive nephritics in Group 1, and such belief will be verified by the further clinical observations of these cases.

**Excess of Cholesterin in Blood in Bright's Disease.** M. Cordier<sup>1</sup> calls attention to this excess in the first stage of Bright's disease before the definite renal alterations appear. The patient whose case is discussed had a large heart, dyspnea; nitrogen-content of urine normal, that of blood very small. The amount of cholesterin in the blood was enormous—6 gr., 40 per 1000. Vegetable diet quickly led to steady improvement. This excess of cholesterin is in relation, Cordier says, to the adrenal hypersecretion, and has a great importance in the beginning development of interstitial nephritis.

<sup>(1)</sup> Presse méd., Dec. 17, 1919.

**Acute Unilateral Hematogenous Nephritis.** In this brief discussion and presentation of clinical records of patients with unilateral hematogenous nephritis, the condition named above, J. M. Maury,<sup>2</sup> of Memphis, states that while infection of the kidneys are usually described under the names of pyelitis, pyelonephritis, pyonephrosis and perirenal inflammation, it must be kept in mind that they are but different stages of the same process, and have no sharp line of distinction between them. Acute unilateral hematogenous nephritis is described as an acute septic blood-borne infection, because it is in one kidney, the exciting cause being one of the pyogenic organisms. The disease begins with the lodgment of a single organism or a single group or organisms in the cortex of the kidney. From the primary focus the infection is spread to the lymphatics, blood-vessels and tubules more or less throughout the organ.

The symptomatology is marked by onset that is sudden and is usually manifest as severe pain in one or the other side of the abdomen, more frequently the right.

The pain is usually severe and is accompanied with nausea, vomiting, rigidity of the abdominal muscles of the corresponding side, rise of temperature, and increased leukocyte count. Frequently a diagnosis of acute appendicitis, acute cholecystitis, or perforation of a gastric or duodenal ulcer is made as a mistake. The urinary findings are a trace of albumin and a few red and white cells. The suppurative type gives rise to an increased septic intoxication, with continued high fever, rigor, sweats and delirium, while in the non-suppurative type, the symptoms gradually become less intense with the lowering of temperature, less leukocytosis and a gradual improvement in the patient's condition.

Under the heading of treatment, the author says that in the non-suppurative cases on milk diet, large quantities of water and hexamethylenamine, recovery will ensue, while in the suppurative type only surgery will save the patient's life. If the process is limited to one pole excision of the diseased portion of the organ has, in many cases, resulted in cure. This, however, because of the difficulties of determining the extent of involve-

---

(2) Southern Med. Jour., September, 1919.

ment of the organ, is a questionable procedure, and it would seem that unless contraindicated by some uncertainty as to the condition of the other kidney which would make it advisable to conserve all kidney tissue possible, nephrectomy would be safer.

**Diet in Renal and Circulatory Disease.** A discussion of diet in renal and circulatory disease, is presented by P. Bergoignan,<sup>3</sup> of Paris, France.

Taking the physical signs and the condition of the renal function as guides, this subject may be discussed under the heading of acute nephritis, and among the chronic forms, simple albuminous nephritis, dropsical nephritis and hypertensive or uremia-provoking nephritis.

For the first condition, a strict milk diet should be ordered in the following way: The amount should never exceed 2.5 liters in the twenty-four hours, beginning with 1 liter; 300 c.c. should be taken in spoonful every three hours, flavored with a little coffee or tea. After each feeding of milk, the mouth must be well washed out with some alkaline water. Skimmed milk, clotted milk, or kephir may be allowed according to the nature of the case. After a few days on this diet, it is advisable to modify it by reducing the quantity of milk to 2, or even to 1.5 liters, and allowing 100 gm. of biscuit and 80 gm. of sugar. Later, various farinaceous foods or decoctions of cereals may be given.

After the acute stage has passed off, and the case has become one of simple albuminous nephritis, a meat and vegetable diet not deprived of chlorides should be given. Meat, red or white, is allowed in small quantities, provided it is quite fresh and well-cooked so as to avoid toxins. This permission applies as well to fish and eggs. All kinds of vegetables are allowed, but care must be taken to limit the amount of dried vegetables and of acid fruits and vegetables if there is any tendency to oxaluria. Milk is useless as a remedy, and it is often necessary to reduce, or even entirely to suspend its use when patients believe that in consequence of their albuminuria they ought to take as much of it as possible.

A chloride-free diet is called for in a chronic dropsi-



cal nephritis. It is useless and even harmful in simple albuminous nephritis, and is insufficient in the uremia-provoking forms.

A strictly chloride-free diet, only introduces about 1.5 gm. a day, an amount which is always well within the capacity even of badly damaged kidneys to excrete. All food must be prepared without salt. Table salt must be strictly forbidden, likewise all salted meat and salt-water fish. Bread must be made without salt. Foods should be flavored with spices, oil, fresh butter, vinegar, lemon juice or sugar, as may be found suitable.

The dechloridation process can be furthered by various means, such as rest in bed, theobromine, and drastic purgatives, in order that the duration of the course may be shortened. In a short while it will be possible to add to the food a definite quantity of salt each day.

The diet with little nitrogen is the most difficult of all. Fortunately it is only necessary in cases of uremia provoking nephritis, in which the outlook is grave. It comprises all degrees of severity from the reduced amount of protein to a complete prohibition, and even to the point of absolute fasting. As, however, there is always retention of chlorides, as well as of nitrogens, the diet is deprived of chlorides and of nitrogen at one and the same time.

All animal food, eggs, dried vegetables, and potted meats must therefore be strictly forbidden. About 200 gm. of salt-free bread may be allowed each day, and only just enough milk to prepare certain dishes. The patient must obtain his nourishment chiefly from rice, potatoes, tapioca, sago, arrowroot, fat, plenty of sugar, all kinds of green vegetables, carrots, parsnips, and all sorts of fruit. As it is very hard to submit to this diet, every opportunity must be taken to abate its rigor. If there is only slight retention of chlorides, a little salt may be allowed. As soon as there is less retention of urea, it will be possible to give at long intervals a little potted meat, an egg, or a little meat. If, on the other hand, the case gets worse, it will be necessary to restrict the intake to fruit for several days, such as 3 or 4 kilos of grapes a day. If, finally, an attack of uremia seems imminent, all food must be cut off for four days, giving

nothing but 2 liters of pure water or Evian water, and an active purgative every morning.

The diet suitable for uric lithiasis differs in no way from that for gout, and is, therefore, poor in nitrogen.

The quantity of fluid to be allowed to patients with defective excretion of urine, is an important matter which often proves a difficult one. In mild cases of edema due to retention of chlorides, the amount should be reduced to 1,000 or 500 c.c. in the twenty-four hours. In bad cases of cardiac dilatation, fluids should be entirely suspended for one or two days. This step alone may succeed in bringing about considerable diuresis. At a later stage, the maximum amount allowed should not exceed 1,000 or 1,250 c.c.

In uremia-provoking nephritis, in order to carry off as much urea as possible, from 1.5 to 2 liters of water are necessary. In lithiasis, the patient ought to take from 2 to 2.5 liters of fluid in the twenty-four hours.

## DISEASES OF THE GASTRO-INTESTINAL TRACT

**Diagnosis of Gastro-Intestinal Diseases.** That there is perhaps no field in medicine more burdened with unproven theories than that of the diseases of the gastro-intestinal tract is the introductory statement of C. W. McClure,<sup>1</sup> of Boston, in his article dealing with certain diagnostic aspects of medico-surgical diseases of the gastro-intestinal tract.

The work carried out on patients referred to in this article was done in the medical clinic in the Peter Bent Brigham Hospital, in Boston. Because of the difficulties in exhaustive study and experimental work on disease in this part of the body, there is frequently a lack of knowledge, first, of the etiologic factors of gastro-intestinal diseases, and second, of the pathologic physiology of these diseases.

The radiographic fluoroscope is looked upon by McClure as a method available for settling many disputes and solving many problems in this field of medical practice. It is his impression that the value of the fluoroscope and of a certain number of fairly common fluoroscopic findings are not generally known, or if they are known, their importance does not seem to be appreciated.

By the use of the fluoroscope the stomach itself is examined for a residue of a barium meal given six hours previous to the examination, for the different types of peristalsis, especially hyperperistalsis, for focal areas of abnormal muscular contractions in the walls of the stomach, for spasms and deformities of the stomach walls, and for abnormalities in the size, shape, and the position of the stomach. The first portion of the duodenum leading off from the stomach, the so-called duodenal cap, is examined for deformities in its outline. The remainder of the gastro-intestinal tract is not considered in this paper.

(1) Boston Med. and Surg. Jour., Sept. 25, 1919.

Two phenomena accompany the majority of abnormalities seen by means of the fluoroscope. These are the functional muscular phenomena of over-activity on the one hand, and atony on the other; and second, actual structural changes in the walls of different parts of the alimentary canal. It is recalled, however, that the diagnostic status of many muscular phenomena as seen through the fluoroscope is not definitely settled. The best known of the muscular phenomena are hyperperistalsis, the spasm producing an incisura, and atony. The clinical significance of spasms and of hyperperistalsis in the stomach are prone to be neglected by internists and surgeons alike. These conditions may not be diagnostic of any lesion in themselves, but a certain number of them furnish confirmatory evidence that at times is of the utmost aid in diagnosis.

The record of a patient who had carcinoma of the esophagus is cited. The Roentgen report states that the esophagus was slightly dilated. The swallowed barium stopped in the region of the cardia. This portion of the esophagus was irregular in outline. A little barium trickled through into the stomach. Visible peristalsis was seen in the esophagus and at times it was reversed in type.

A second instance cited is one of cardiospasm, in which six hours after the barium meal there was seen a large somewhat fusiform, sharply defined shadow overlying that of the heart. Its lower extremity was conical in shape. A small quantity of the barium meal had reached the stomach. At the cardiac orifice of the stomach there was an almost complete obstruction, only a fine stream of barium was seen to run through it into the gastric cavity. The findings were those of marked dilatation of the lower end of the esophagus, due to cardiospasm.

A third instance cited is that of ulcer of the stomach. Here the stomach was normal in position and tone. It was freely movable. There were hyperperistalsis and a small six-hour residue. In the antrum near the sphincter was a small area in which peristaltic waves did not occur. This same condition persisted on two examinations made at twenty-four hour intervals. The

duodenal cap came off at one side of the sphincter. The cap itself was normal in position and in outline.

In another instance of questionable gastric ulcer, the stomach was normal in position, tone, and outline, and was freely movable.

The peristalsis was irregular and sluggish; at times three waves were visible. There was a small six-hour residue. On the lesser curvature, proximal to the antrum, there was an area in which no peristalsis occurred, although peristaltic waves were seen to pass over the greater curvature opposite this area. The same phenomena were noted on a second examination one week later. There was no irregularity in outline of the stomach. A good sphincter and first portion of the duodenum were seen.

McClure says that the two instances of involvement of the cardiac orifice of the stomach represent well the different pictures produced by muscular spasm and actual structural deformity. In the case of cardiospasm, the greatly dilated esophagus was smooth in outline. In the case of carcinoma, the esophagus was but little dilated and its lower end very irregular in outline.

In the diagnosis of lesions in the cardiac end of the stomach, the fluoroscope is considered by McClure to be of indispensable value. Often lesions in this region are not visible in the radiographic plates after the stomach is filled with the barium meal; or the gas bubble in the fundus may prevent that region from filling with the barium salt, and hence no irregularities are manifested. One of the most important parts of the radiographic examination is the observation of the barium meal as it enters the stomach. Lesions high up on the lesser curvature frequently cause marked swirls in the barium stream as it falls through the cardiac orifice, which are diagnostic evidences of a growth in that region. Structural deformities, due to perforating ulcers, may be seen at this time, while after the stomach has filled they may not be visible. Neoplasms involving the top of the fundus of the stomach may best be demonstrated by the fluoroscope after filling the region with the barium meal. The demonstration is made possible by the fact that the inspiratory contraction of the dia-



phragm presses on the fundus of the normal stomach and causes it to assume a very different shape from that found during expiration. A new growth in the fundus may stiffen its walls and prevent these changes in shape from occurring.

The factors in the fluoroscopic picture which are significant of ulcer are hyperperistalsis, an incisura, a residue six hours after the barium meal, and a deformity of the stomach walls.

Instances arise in which the clinical findings render a diagnosis of gastric ulcer exceedingly questionable, but the radiographic findings in such cases may strongly indicate gastric ulcer. In such cases it seems wise to McClure to institute medical treatment for ulcer and to allow the progress of the case to govern further therapeutic measures.

The author considers it unfair, usually, to ask the radiographer for more than a description of his *x-ray* findings and for suggestions as to their meanings. It is important that physicians learn to interpret the roentgenologic findings in relation to the clinical symptoms in a given case, in order to glean the most benefit from *x-ray* studies.

In referring to spasms of the musculature of the gastro-intestinal tract again, McClure states that these may be due to extraneous causes, either functional or organic. Extrinsic spasm is commonly differentiated from intrinsic spasm by the fact that the former is usually not present on a second examination, and that it almost invariably disappears after the administration of atropine.

The record of patients is presented to demonstrate this finding.

Antiperistalsis or reversed persistalsis invariably points to some lesion in the gastro-intestinal tract which is usually, but not always, obstructive in type. It may accompany a gastric lesion remote from the pylorus. Antiperistalsis occurring above a perforated gastric ulcer situated on the lesser curvature some distance from the pylorus was observed by the author and McCarty. Antiperistalsis can, of course, be demonstrated only by the fluoroscope. A further thought in regard to this work

is that operations on the stomach and intestines should always be followed by a detailed fluoroscopic report and radiogram of the regions operated on a month or two after convalescence has been established. If a question of a new lesion arises, perhaps several years afterward, the abnormal conditions resulting from the operation may make the interpretation of further radiographic studies difficult or even impossible.

Another phase of the gastro-intestinal field is the use of diet and medication in the diagnosis of these disorders. Practice in this field varies extremely. For instance, diet for ulcer varies from the high caloric meat-containing *régime* of Lenhartz, through the milk and alkali treatment of Sippy, to the starvation method of Leube; just as radical differences exist in the treatment advised for other conditions such as hyperacidity, hypersecretions, chronic dyspepsia, etc. Because of this great variation in practice, the author made a study of the reaction of patients with certain of the gastro-intestinal disorders to a wholesome general diet. From the results obtained, he states that in every case in which it was proved that a patient could not eat with comfort a diet rational for a healthy person leading about the same mode of life, some apparently definite underlying cause was found. The most common of these causes have proved to be, first, functional nervous conditions, second, organic diseases either of the alimentary tract, or other organs, or constitutional in type, and third, introduction into the system of toxic substances—lead, mercury, etc.

So far, it has been possible to interpret hyperacidity, anacidity, hypersecretion, chronic dyspepsia, etc., as symptoms of some underlying cause. Until the basic cause has been definitely established the use of drugs and diets has certain evils: they may alleviate, even in organic disease, the gastro-intestinal symptoms. The assumption is then prone to be made that the case is purely functional in nature and further investigation into its cause is neglected.

It is shown next that patients with certain lesions of the stomach, such as carcinoma of the lesser curvature, may remain free from symptoms if they are put

upon a well-regulated diet of soft and palatable food, and that unless a fluoroscopic examination is made, or *x-ray* plates of the stomach made, an error in diagnosis will exist. Not infrequently, special dieting with or without antacids relieves the symptoms, their ultimate cause is not considered an important matter, and the physician is led to overlook what may be the first signs of the return of the former trouble. For this reason if such a patient can not eat a wholesome general diet, the reason should be ascertained.

This discussion is not to be construed, McClure says, as meaning that certain drugs and methods of special dieting are never of value, but it is for the purpose of emphasizing, first, that symptoms valuable for diagnostic purposes may be masked by the too early use of these therapeutic measures and, second, that an attempt should always be made definitely to establish the underlying cause for gastric symptoms.

[This article embodies very rational principles and splendid common sense conclusions. It deserves wide dissemination and careful reading by every practitioner who desires to afford the patient with gastro-enteric disease proper management.—B.]

**The Use of X-Rays in Gastro-Intestinal Diagnosis.** In this article on the use of *x-rays* in gastro-intestinal diagnosis, H. E. Cheney,<sup>2</sup> of Montreal, discusses first the variety in number and quality of questions asked by physicians who send their patients for *x-ray* examination. In making a barium meal examination, Cheney has the patient report not later than 10 o'clock without any breakfast and without any purge the night before. There is no objection to the patient having a cup of tea and a piece of toast about seven o'clock, and in most instances, it is preferable as it prevents headache, and does away with the violent hunger peristalsis of the stomach.

Gastro-intestinal conditions are diagnosed by summing up the findings in the fluoroscope and skiagraphs after the patient has taken the prescribed barium meal, which consists of 4 fluid ounces of barium sulphate mixed with water, to the consistency of thick cream, and 8

(2) Canadian Med. Ass'n Jour., March, 1919.

ounces of buttermilk. Sweet milk may be given if the patient objects to buttermilk.

Considering ulcer of the stomach first, Cheney says that the findings that point to ulcer may be summed up under two headings:

*A.* Positive signs.

*B.* Possible signs.

The positive signs produced by an ulcer are tabulated as follows:

First is the barium-filled cavity: This may take the appearance of a wart-like shadow outside the general outline of the stomach, and is caused by an ulcer crater being filled with barium and silhouetted on the screen or plate. This is only established by appearing during a long fluoroscopic examination, or on a series of plates, and may appear in any part of the stomach or the duodenum.

A second positive point is barium passing through perforation: This may be an acute perforation and passing immediately into the peritoneal cavity or only between the muscular coats of the stomach, or it may be an old perforation which has been walled off, forming a pocket or pouch in the adjacent tissues.

A third condition is pyloric obstruction: An old ulcer with a cicatrix producing obstructions, which if complete, or even if a ten-hour retention is present, causes the barium to drop nearly to the pubis in a large dilated stomach forming a saucer-like pool, with a sharp line of demarcation between it and the lighter fluid above, which has remained in the stomach from the night before. Within a few minutes after this takes place, in the majority of cases a very violent persistalsis will be established, with very little if any effect. This lasts for five or ten minutes and then subsides. This process continues intermittently until the stomach is empty, or until reverse peristalsis takes place or a stomach tube is used.

Fourth positive sign is the permanent hour-glass stomach. In this condition the barium fills the upper bulb and remains there for a time, varying from a few seconds to five or ten minutes, when peristalsis is established and forces the contents into the lower bulb, which is of

itself usually proportionately more tardy in emptying, taking from two to ten hours or more.

This retention at the pyloric end of the stomach, or in the lower bulb, is due to the arrest of peristalsis by the cicatrix at the site of the hour-glass constriction. In these cases, a duodenal cap is very seldom formed owing to the amount of barium forced through at one time being too small to fill the first part of the duodenum.

The fifth and last positive sign described is the incisura. This occurs at each filling of the duodenum or, if in the stomach, after the stomach has been filled. Incisura, or filling defects, may occur in the duodenum, and if permanent in a series of plates, or if examination shows the presence of an old ulcer, at the point where the defect is found. In acute or irritable cases, the incisura appears on the opposite side of the duodenum and is caused by a spasmodic contraction of the muscle wall.

In the cases of irritable gastric ulcer, the stomach fills out properly at first and in a few seconds the examiner will notice an incisura appear slowly in the outline, usually of the greater curvature of the stomach.

The first point considered under possible signs is the duodenal cap.

The presence of a good duodenal cap is sufficient evidence of a normal duodenum, but the absence of a cap or any temporary imperfection may be caused by one of many things, as adhesions, pressure from gall-bladder or from other causes, neoplasm or tumors in adjacent tissues, tension caused by weight of food in a ptosed atonic stomach, cicatrix from old ulcer, etc. Also, retention, caused by a cicatrix, atony, adhesions, pressure from without caused by abnormalities in adjacent tissues, etc., is a possible sign.

Further signs are rapid emptying, caused by hunger peristalsis, gastric neurosis, gastritis, irritation from without the stomach, etc., and such causes.

These constitute the possible signs of ulcer.

The author states that six hours seems to be the maximum time for the normal stomach to hold its contents: but four hours is about the average time that should elapse before the stomach is completely empty, and in



seven hours from the ingestion of the meal or three hours from the emptying time of the stomach, the ileum should be emptied. Frequently the barium does not remain in the ileum any appreciable length of time, and this condition usually points to one of two things—enteritis, or sub-acute appendicitis. Delayed emptying time may be caused by cicatrix, neoplasm or other causes of retention, or a chronic appendicitis.

When obstruction is observed in the colon, surgical measures are usually imperative at once. At the end of twenty-four hours the barium should be for the most part beyond the splenic flexure.

**Therapeutic Test for Differentiation of Gastric and Hepatic Disorders.** Discussing this subject, G. Leven<sup>3</sup> observes it was referred to as far back as 1784, by Pujol; and one hundred and thirty years later was still attracting attention (Loeper).

According to some authors the gastric symptoms from gall-stones preponderate; and others state that gastric ulcer may be thought to be cholelithiasis (Bouveret).

Anatomy teaches us the connections of the large bile-passages, the gall-bladder, and the pyloro-duodenal region. It is not surprising that owing to the close relation of these structures it is difficult to pick out the exact region involved, especially as one organ is almost sure to react on its neighbor; it is very uncommon not to find adhesions surrounding the duodenum and pyloric region when the gall-bladder is involved or *vice versa*. The normal physiology of the liver and stomach show us also that altered function in one is sure to react on the other, when the functional trouble is not "contemporaneous," as it should be in the majority of cases. Pathologic physiology explains all the reflex symptoms whose point of departure is sometimes the stomach and pylorus, at others the gall-bladder with the cystic and common ducts, or again the duodenum. The physician should not be surprised that in certain cases with obscure symptoms, the picture is sometimes that of a gastric disorder, sometimes that of a hepatic one.

Leven has seen patients with biliary calculi, without

(3) Presse méd., Nov. 15, 1919.

icterus; and others in whom the calculi were findings at necropsy, because no cholecystitis had been produced.

This brief enumeration shows the difficulties in diagnosis and since pathognomonic signs are to be found neither in the spontaneous remissions of the painful crises, the localization of pain in the hepatico-vesiculo-duodenal area (which is also the pyloro-duodenal one), in the condition of permanent nausea, nor in the time of the crises, all signs to which authors attach too much importance, we are led to call for the therapeutic test for differential diagnosis.

Such a test should play a double rôle, if efficacious, we can eliminate the idea of a hepatic lesion (cholecystitis or calculi), and a gastric disorder with lesion. If efficacious also, we have the proof that we are dealing with a grave, complicated dyspepsia but without any organic lesion necessitating a surgical operation.

When this test is efficacious, we have to treat a medical affection; in the contrary case, the surgeon must intervene.

This therapeutic test Leven says will solve the problem in three or four weeks. After the first ten or fifteen days, progress is clear, but we must not anticipate the final result. After the interval mentioned, if there are no results, we can tell the surgeon to investigate the hepatico-vesiculo-duodeno-pyloric region, and that he will discover there calculi, cholecystitis, or a pyloric or a duodenal lesion. As a general thing, he will uncover complex lesions, involving all these regions more or less.

The following principles form the base of this therapeutic test: Restricted diet to assure rest of the stomach for the first few days, less restricted during the days following, from the fourth or fifth on, the nature and quantity of both solids and fluids being chosen.

In the first (restricted) period, the patient ingests in twenty-four hours, 1500 gms. of warm infusion the first day; 850 gms. of milk with 750 gms. of *ptisane* the second day, 1500 gms. of milk on the third. In the next—or less restricted—period, a choice of aliment is available.

In addition to this regimen, the most absolute physical and mental repose must be observed, the patient stays in bed for the first few days, even a week, and his physical

efforts are reduced to the minimum in the following weeks. Intellectual rest as well is necessary, and marital relations are to be abstained from.

All medication is suppressed for the first three days, then sodium bromide is prescribed systematically, 2 gm. daily, each spoonful being taken in the course of the two principal meals, for a period of twenty days. Addition of a potion of bismuth (carbonate of bismuth, 10 gm., gum arabic, 20 gms.; sterile distilled water, 300 gms.) is not to be made till after isolated use of the bromide for four or five days, and in cases in which its action does not appear efficacious.

The bismuth potion is to be taken from 7 a. m. to 9 p. m., in soup-spoonful-doses, every  $1\frac{1}{2}$  hours for the first three days; every two hours for the next five days; and every  $2\frac{1}{2}$  hours for the following five days, lessening the amount little by little, according to the progress, without stopping altogether, over a period of twenty days. No attention, as a rule need be paid to the constipation which is not set up by the bismuth. However, if it be prolonged, say for three or four days, laxatives must be prohibited, also purgatives and even enemas with more than 500 gms. of fluid. The ones to be used are of water 400 gms., milk, 100 gms. injected slowly and not under pressure.

The bromide and the bismuth act on the element of pain, on the spasms, on the whole of the reflex symptomatology, and consequently it is indispensable to avoid producing new reflexes by using therapeutic means which may be far from innocent.

During the time spent in bed, then at night for the following days, hot moist applications to the abdomen are necessary. They should be kept up six hours a day besides the nightly use when the stay in bed ends.

In short, the measures proposed—very trivial though they may seem—have for their object the observation of the patient himself, the reduction of the manifestations to the symptoms of the disease alone, and the suppression of the symptoms superadded by too-numerous therapeutic efforts. Observation, reduction, and suppression are all realized as completely as possible by the above described technique.

[This article contains no statement of the use of clinical laboratory tests (test meals, x-ray and the like) to arrive at a diagnosis. If these diagnostic resources are efficiently applied the therapeutic test outlined would be of very little utility.—B.]

**Effects of Restricted Diets on Gastric Secretion and Motility.** Working in the medical services and the pathologic laboratory of the Mt. Sinai Hospital, New York, B. B. Crohn<sup>4</sup> and Joseph Reiss have carried out a study on the effects of restricted so-called ulcer diets on gastric secretion and motility. Various phases of the work are discussed separately and in detail and many of the results are presented in graphic charts. The results obtained, and their significance, however, are all brought out clearly in the discussion by the authors. Here they attempt to estimate the relationship between clinical relief from symptoms and physiologic or chemical benefit.

They ask: Does medical treatment reduce the hyperacidity of ulcer, and if so, is this relief responsible for the clinical improvement? Also, does restricted diet cause the disappearance of hypersecretions, and if it does, is this the factor that relieves the symptoms? Finally, can delayed motility in the presence of ulcer be relieved by the eating of small quantities of food often repeated, and if so, is this the factor that brings about apparent cure of symptoms?

In the present work medical treatment resulted in a net reduction of acidity in thirteen out of a group of thirty-four patients, 38 per cent. If only those cases with definite hyperchlohydria are considered, omitting all cases with isosecretory or hyposecretory curves, the percentage of net lowering of acidity is still lower—30.3 per cent.

Of these thirteen individuals chemically benefitted, twelve, or 92 per cent. were discharged free of symptoms. Loose reasoning might lead one to see a relationship of cause and effect in these figures, but if the cases in which treatment failed to invoke chemical relief are analyzed and these comprise the larger proportion, there is found despite this fact, clinical relief in thirteen, or 62 per cent. In other words, of twenty-five persons discharged from

(4) Amer. Jour. Med. Sci., January, 1920.

the hospital free of symptoms and apparently well, thirteen, half the number, retained the same height and type of acidity as on admission. If clinical cure depended on relief from hyperacidity, then the optimum result should be in this class of cases. Almost 80 per cent. of patients with hypochlorhydria left the hospital practically relieved, yet only 30.3 per cent. of these showed chemical relief from the excessive acid production.

Two inferences may be drawn from these figures: First, only a small percentage of ulcer cases react to medical treatment by showing a reduction of acid produced during digestion, 38 per cent.; and second, clinical improvement can take place independently of whether the hyperacidity is relieved or whether the case remains acid.

As regards hypersecretion, a similar conclusion is soon arrived at. Twenty cases in this group showed hypersecretion. In nine, or 45 per cent., medical treatment caused the disappearance of this abnormal factor. In the other eleven, or 55 per cent. of the cases, medical treatment failed to alter the hypersecretion, yet, 80 per cent. of these patients left the hospital apparently well. Exactly 50 per cent. of the clinically cured patients still retained hypersecretion on discharge from the hospital, and yet subjectively the pyrosis, heartburn and pain had disappeared.

From these figures again two conclusions may be drawn: First, medical treatment, consisting of restricted diet and rest in bed, causes the cessation of hypersecretion in 45 per cent. of the patients, a fair proportion; second, clinical improvement takes place as often in patients with persistent hypersecretion as in those relieved of the excessive flow of gastric juice, and is apparently not dependent upon it.

Finally, the relationship between improved gastric motility and clinical relief is considered. There were thirteen cases of delayed motility; in eleven or 85.4 per cent. medical treatment succeeded in alleviating this symptom and reducing the emptying time to normal. All these eleven patients were in addition freed from subjective complaints. Two cases resisted treatment;



motility was not improved and these patients were discharged clinically unrelieved.

There are no instances of clinical cure that could be attributed solely to reduced acid secretion when delayed motility was present as the complicating factor. Unless relief is had from the pyloric spasm, one fails to note the disappearance of subjective symptoms.

In considering what change in the physiology or pathology of the stomach can be held responsible for relief from symptoms in cases not complicated by pyloric spasms, the authors say that the answer must be sought and will probably be found in the radiographic studies of Ginsberg, Tumpansky and Hamburger, Carlson, Hardt and others. These authors have demonstrated the close relationship between subjective pain and exaggerated peristalsis or hunger contractions. It is quite likely that restricted diet and bed rest have a quieting influence on gastric contractions, diminishing the amplitude and the violence of these contractions. Reduction of acidity and secretions may or may not accompany the reduced tonus of the stomach.

**Therapeutics and Gastro-Intestinal Disorders.** The term "indigestion" is used by D. Vanderhoof<sup>5</sup> in discussing therapeutics and gastro-intestinal disorders to designate the complaint of patients with symptoms referable to the stomach, bowels and abdomen in general. He emphasizes the fact that the term "indigestion" in itself is meaningless and is a detriment to medical nomenclature, but because of the firmness with which it is fixed in the minds of patients it is used by the physician, but not nearly so frequently as by the patient in giving a history. The present report is based on the records of 2,000 patients seen by the author whose complaints were attributed to some disturbance of digestion, such as stomach trouble, dyspepsia and abdominal pains, flatulence, vomiting, etc., and entirely exclusive of patients complaining of other symptoms who were found, on examination, to have some lesion of the gastro-intestinal tract.

The accompanying chart has been prepared indicat-

(5) Med. Record, Sept. 29, 1919.

ing the frequency and proportion of the diseased conditions found in these patients.

CAUSES OF "INDIGESTION"—ANALYSIS OF 2,000 CASES.

	Cases	Per Cent.
1. Chronic appendicitis .....	436	21.8
2. Chronic cholecystitis .....	224	11.2
3. Neuroses .....	218	10.9
4. Peptic ulcer .....	206	10.3
5. Kidneys, affections of.....	137	6.8
6. Achylia gastrica (uncomplicated).....	81	4.0
7. Visceroptosis .....	69	3.4
8. Lungs, affections of .....	60	3.0
9. Heart, affections of .....	50	2.5
10. Cancer of stomach .....	46	2.3
11. Blood and ductless glands, affections of...	44	2.2
12. Enterospasm (mucous colitis) .....	40	2.0
13. Peritoneal adhesions .....	38	1.9
14. Female pelvic organs, affections of.....	35	1.7
15. Eyes, affections of .....	32	1.6
16. Migraine .....	26	1.3
17. Central nervous system, organic disease of	22	1.1
18. Cancer of intestine.....	21	1.0
19. Infectious diseases .....	19	0.9
20. Liver, affections of .....	18	0.9
21. Ears, affections of .....	16	0.8
22. Enterogenous toxemia .....	11	0.5
23. Miscellaneous conditions .....	114	5.7
24. Diagnosis not made.....	37	1.8

In the study of the second thousand patients included in this chart, the fractional method of gastric analysis was employed, as well as routine Wassermann tests of the blood serum in each case. In addition to the possible margin of error in these figures, certain patients presented more than one lesion that might have acted as a reflex cause of indigestion. In such instances, the author has tabulated according to his discretion the one that seemed most likely to be responsible. Included under miscellaneous conditions in the table are such diseases as pellagra, amebic dysentery and malaria, together with focal infections of the tonsils and teeth, and instances of cyclic vomiting, intestinal parasites, cardiospasm, diverticulitis, peritoneal tuberculosis, cancer of pancreas or esophagus, retroperitoneal sarcoma, hypertrophic spondylitis, etc.

Vanderhoof states that the chief symptoms presented by the patient with chronic or recurring indigestion are comparatively few and limited. He classifies them as follows: Loss of appetite, coated tongue, nausea and vomiting, pyrosis and sour stomach, flatulence and visceral pain.

Under the heading of treatment of indigestion he emphasizes the great importance of finding and eradicating the underlying cause. The popular idea of restricting the diet of every patient with indigestion is not only a fallacy but may be largely responsible for the continuation of the symptoms. A brief consideration of such a tabulation as that presented in this article is considered to suggest at once a treatment to be adopted in such instances.

**The Physiology of Nutrition.** This article by W. M. Bayliss,<sup>6</sup> Professor of General Physiology at University College in London, is one of a series of articles on diet in health. This discussion by Bayliss deals with the fundamental principles of nutrition, making very clear the processes of digestion.

He says that the purpose of food is two-fold—on the one hand, to serve as material out of which the structures of the body are produced, and, on the other hand, to afford the energy required for muscular work by being burned up or oxidized. It is the latter purpose for which the larger part of food is needed at all ages. The former is naturally more evident in the growing animal than in the adult; indeed, the amount actually required to replace the wear and tear of the active tissues is very minute.

In considering the value of food material, one should keep in mind clearly the unit of food value as it is rated for body use. This unit is the calorie, and is that amount of heat energy required to raise the temperature of one kilogram of water by one degree centigrade.

A certain quantity of energy is consumed by the heart and the muscles of respiration and there is a certain loss of heat from the skin during sleeping hours. The combustion processes needed to supply this are known as the basal metabolism. It may be taken as being very

nearly one calorie per kilogram of body weight per hour, or 1700 calories a day for a man of 70 kilograms or 175 pounds.

The degrees of work may be defined by the excess of energy supply needed over and above that for basal metabolism. Taking the work of a tailor as light work, his food must provide altogether 2500 calories a day, but since the whole of the food bought is not digested and utilized, 10 per cent. must be added, making 2,750 calories. A metal worker needs 3,500, and a wood sawyer 5,500.

To give a concrete meaning to the figures, the following brief table is presented, showing how many grams of different foods are required to furnish 100 calories:

	Gm.
Butter .....	13.5
Cheddar cheese .....	22.
Sugar .....	24.5
Oatmeal .....	28.
Mutton .....	29.
Fish .....	67.
Eggs .....	68.
Milk .....	145.

28.35 grams equal 1 oz.

The actual materials available for food are proteins, fats, or carbohydrates. All these contain carbon, hydrogen and oxygen, but proteins alone contain nitrogen.

In order to make new tissues, or replace those worn away, nitrogen must be supplied, as well as carbon, hydrogen and oxygen. Proteins in order to be utilized by the tissues must be split up into their constituent amino-acids, of which they contain a large variety. This is effected by the digestive enzymes of the alimentary canal. These amino-acids are absorbed by the blood and pass to the liver. Part of them escape the action of the liver and are used by the tissue cells for the purposes of growth and repair. The greater part, however, become "de-aminated." That is, split up into ammonia and a non-nitrogenous part, which has the constitution of a ketonic aldehyde. The nitrogenous part of the protein is of no value as a source of energy. Protein can not be stored in the body except in the form of new tissue structures.

The minimum amount of protein actually necessary in the diet of the adult usually depends on the amount of tissue waste to be repaired. This is very small, as a rule, but a greater quantity than the minimum is desirable at all times. In any ordinary mixed diet there is no need to pay particular attention to the protein contents, a fact which has been expressed by the author in the following statement: "Take care of the calories and the protein will take care of itself."

Seventy grams of protein daily has been designated by Bayliss as the daily ration to be aimed at for an average individual. It should be, especially for the growing organism, of mixed origin, and in part from animal sources.

Under the heading of proteins he refers to the purine derivatives, the nucleins, and their decomposition products, uric acid, and so on. These form components of the nuclei of cells, while the main source of the nuclein required for the cells is that taken in with the food: the organism has the power of synthesizing it from the amino-acids of ordinary protein.

Carbohydrates are supplied in the form of starch and sugar, and they constitute the chief source of the supply of energy. Whatever the form in which they are taken, they must be converted by digestive enzymes into either glucose, fructose or mannose, before the cells can oxidize them. The chief carbohydrates taken as food are starch, cane-sugar, milk-sugar, maltose and, to some extent, glucose in fruit. The chief place of consumption of glucose is the muscular tissue, and it is carbohydrate that is the normal source of the energy of muscular contraction.

Alcohol, although it is burned in the body, gives heat alone, except when taken in very small quantities.

The power of storing carbohydrates as glycogen, although it is possessed by other tissues in addition to the liver, is a limited one, but it can be stored to an almost unlimited extent by being converted into fat and deposited in the subcutaneous tissue.

Although both protein and carbohydrates are necessary, it is at present impossible to make the same statement with certainty in respect to fat. There is, however,



no doubt that it is desirable, if only for the preparation of attractive dishes by the cook. It is a very concentrated form of energy-giving food, and 25 per cent. of the total energy value of a diet should be in the form of fat.

When taken into the alimentary canal it is acted upon by the lipase of the pancreatic juice. It is then split into glycerol and the particular fatty acid united with it. The fatty acid is dissolved by the bile and perhaps partly taken up by the epithelial cells of the villi in the form of droplets. Fats when used for energy purposes are finally burned to carbon dioxide and water, but the intermediate stages are not completely known. When oxidation is incomplete, as in diabetes, acetone bodies are formed, giving rise to the state incorrectly called acidosis.

All three classes of food constituents have their value as sources of energy. One gram of dry material gives, in the case of protein, 4 calories; of carbohydrate also 4 calories; of fat 9 calories. The relative amount of each component recommended, taking the diet for moderate work in the case of a man weighing 70 kilos, or 175 pounds, is as follows:

	Calories
Protein, 70 grams .....	280
Fat, 90 grams .....	810
Carbohydrate, 550 grams.....	2,200
Total .....	<hr/> 3,390

Under the heading of accessory food factors, Bayliss points out that if an animal is fed on a full diet, consisting of pure carbohydrate, fat, and protein, together with water and salt, growth ceases and certain disease states result. Such a diet can be made perfectly adequate by the addition of a very small amount of fresh milk or orange juice. The chemical nature of the substances thus added is unknown, but they are readily destroyed by preservation or by cooking, especially in the presence of an alkaline reaction. Most articles of food in the fresh state contain some or all of them, but fruit and vegetables appear to be the richest source, especially of that one which prevents the occurrence of

scurvy. A certain amount which need not be great, of fresh fruit should be present in every normal diet. Even infants, if fed on cow's milk, should be given a small quantity of orange juice, if the entire absence of scurvy is to be ensured. This is desirable, since cow's milk does not contain a very large amount of the factor, and, if heated, most of this is lost.

There seems to be some number of these factors, but they fall into two main groups. One group is soluble in fats, and found in butter. This is the "fat-soluble A factor." Another group is soluble in water, and is typified by that contained in wheat-germ, and known as the "water-soluble B factor." Both are necessary for growth. The latter factor appears to be that required to prevent beriberi. The former is possibly the same as the antirachitic factor, while the antiscorbutic factor is distinct from either of these growth-factors.

The way in which these accessory factors act is not clear. They do not undergo chemical change in the way of metabolism like the other constituents of food, and appear to behave as catalysts, like enzymes, bringing about changes by their influence from the outside on tissue activities.

The use of cooking is chiefly for the purpose of destroying parasites and microorganisms as well as making food attractive.

The question of fresh air is a difficult one. Oxygen is not usually spoken of as food, although it is the most important of all. But in rooms that seem "stuffy" there is no actual deficiency of oxygen, notwithstanding the undoubted benefits of a free supply of fresh air. It may be that the stimulation of skin nerves serves to keep alive and alert the nerve centers.

It is obvious Bayliss says that muscular exercise when taken for the purpose of recreation involves the consumption of more energy. It might be held that this implies a waste of food, but the benefit to health, and therefore to efficiency as a whole, is amply sufficient to warrant the outlay.

Since part of the food is used up for the purpose of maintaining the temperature, it follows that the supply needed is less in summer than in winter.

**Pneumoperitoneum.** The roentgenologic findings and a few observations on intra-abdominal pressure are recorded by J. Rosenblatt,<sup>7</sup> of the Sanatorium of the Jewish Consumptives' Relief Society, Edgewater, Colorado.

The article is a report of a case of pneumoperitoneum which occurred accidentally while attempting to induce artificial pneumothorax.

In the literature the author was able to find definite record of radiographic findings in pneumoperitoneum in one single instance, and this was in a patient who had subphrenic pyopneumothorax. The scarcity of literature on the subject is considered to be due to the fact that hitherto the value of air as a contrast medium for roentgenologic study has not been properly appreciated.

The patient studied was a man, 32 years old, who had pulmonary tuberculosis. It was decided to induce artificial pneumothorax on the left side of the patient. Puncture was made in the eighth interspace in the posterior axillary line on the left side, and 1000 c.c. of air put into the peritoneal cavity by mistake. Clinical and roentgenographic observations were made on this patient, and the author states that from the clinical viewpoint the most important observation made was the measurement of the intra-abdominal pressure in an apparently healthy peritoneal cavity.

With the patient in the right lateral posture and the needle introduced just below the left diaphragm, the initial manometric reading before any air was introduced was minus 3 cm. of water, on expiration and minus 2 cm. on inspiration, and after 500 c.c. of air were introduced the readings were minus 2 on expiration and zero on inspiration.

Three days later, with the patient in the same position and the needle introduced in the same area, the initial manometric readings were minus 2 on expiration and minus 1 on inspiration, and after 1000 c.c. of air were introduced the pressure rose to plus 1 on expiration and plus 2 on inspiration. With the same procedure repeated about one week later, the initial readings were again minus 2 on expiration and minus 1 on inspiration. The pressure was always negative, and it took as much

(7) New York Med. Jour., Sept. 20, 1919.

as 1000 c.c. of air to raise it to positive; it was higher on inspiration and lower on expiration. The difference between the pressure during inspiration and that during expiration was uniformly 1 cm. of water. The most important roentgenologic observation that was made was the fact that after certain manipulations, the author was able to obtain a definite outline of the spleen and cardiac end of the stomach under the fluoroscope and to obtain a roentgenogram showing a fair outline of the spleen. It is considered fair to suppose that in certain affections of the spleen, liver, or stomach, one might obtain valuable information by introducing a measured amount of air into the peritoneal cavity and observing the outlines of the various organs by fluoroscopy and radiography. Though the fact that this patient did not experience any ill effect may not be sufficient to warrant the safety of this procedure, there is hardly any reason to consider such an operation dangerous when it is carefully done. As to technique to be followed, Rosenblatt thinks that the safest way would be to use the pneumothorax apparatus and follow the same technique as in inducing artificial pneumothorax, the manometer being used to indicate when the point of the needle is in the peritoneal cavity and at the same time to register the intra-abdominal pressure.

#### **Thoracic Aspiration Preliminary to Vomiting in Man.**

H. Paillard<sup>s</sup> observes that nausea—or the first stage of emesis—is set up by increase of intra-abdominal pressure, and lessening of pressure in the thorax, the diminution being produced by contraction of the muscles of aspiration occurring at the same time as closure of the glottis. This phenomenon of thoracic aspiration—the cardia being relaxed—explains the passage of the stomach contents into the esophagus. This aspiration has been proved experimentally in animals by measuring the intrapleural pressure. Paillard was able to establish its presence in man also, by studying a patient with a tracheotomy.

#### **The Significance and Treatment of Hematemesis.**

In the majority of cases, hematemesis indicates some of the following conditions: Esophageal varices, due to

(S) Presse méd., Jan. 28, 1920.

disease of the liver or spleen, or cancer of the stomach, or peptic ulcer.

Some of the rare causes are: Poisons such as arsenic, phosphorus, corrosive sublimate and phenol; constitutional diseases such as scurvy, hemophilia, Bright's disease, and those diseases of the bile ducts associated with jaundice; specific fevers such as yellow fever, smallpox, measles and influenza.

The mortality in hematemesis is rated variously at from 0.5 to 3 per cent. Moynihan is quoted as stating that only 3 per cent. of cases are amenable to surgical relief.

The tendency in this condition being toward recovery, as coagulability of the blood increases while the hemorrhage continues, the effects attributed to the action of drugs may be questioned. However, the following measures are advised by P. T. Bohan<sup>9</sup> as the most rational treatment of sudden, profuse gastric hemorrhage.

No food by the mouth for forty-eight hours. Water, 1 ounce every half hour. Water may also be given by proctoclysis or by hypodermoclysis. Ice by the mouth may be harmful by exciting peristalsis of the stomach.

Codeine, gr. 1, or morphine, gr.  $\frac{1}{6}$ , hypodermically if necessary for restlessness or fright.

Adrenalin chloride 1:1000 solution, 1 dram in two or three times as much water, every hour or two for two or three doses. It should not be given hypodermically.

Silver nitrate, gr.  $\frac{1}{4}$ , in one dram of peppermint water every three hours for four doses. This, as all remedies, should be given immediately after vomiting.

Alkalies are extremely important to protect the thrombus in the bleeding vessel from the digestive properties of the gastric juice. A powder containing 20 grains of sodium bicarbonate, 3 grains of magnesium oxide and 5 grains of bismuth subnitrate should be given every hour, day and night, for forty-eight hours.

Coagulen, a powder prepared from blood platelets, may be given by the mouth in doses of from 1 to 2 ounces of a 10 per cent. solution.

Lavage is indicated only when there is marked disten-

(9) Jour. Kansas Med. Soc., December, 1919.



tion of the stomach as the gagging due to introduction of the stomach tube may be harmful.

Blood transfusion may be done if the blood-pressure drops to 80, or if the hemoglobin drops to 25, or if the hemorrhage continues in spite of other measures. In cases of emergency, a healthy blood relative can be used as a donor without tests for hemolysis or agglutination.

Measures to prevent recurrences of hematemesis depend largely on the correct diagnosis of the etiology of the hemorrhage. Surgical indications in recurrent hemorrhages from the stomach are limited to two conditions:

First: Splenic anemia. For this condition splenectomy is the recognized treatment, and the results are fairly good, even after the development of ascites due to Banti's cirrhosis.

Second: Cirrhosis of the liver. Here, W. J. Mayo, is quoted as having removed the spleen in six cases of cirrhosis with one death and apparently good results in the other five.

In peptic ulcer, recurrent hemorrhages are due to the corrosive action of the gastric juice. The treatment in this condition should be medical and is covered in the outline given above.

For forty-eight hours following a severe hemorrhage, it is best not to excite peristalsis by any kind of food. The acidity can be controlled by alkalies given every hour day and night. On the third day, milk and cream, one ounce of each may be given every hour from 7 a. m. until 9 p. m. The alkaline powder is given midway between feedings and three powders thirty minutes apart after the last feeding. After a few days, the diet may be increased gradually, but hourly feedings and alkalies between must be kept up for from eight to twelve weeks. Following the plan advised by Sippy, clinical experience proves quite conclusively that the Sippy treatment, if properly given, is the only rational treatment for bleeding ulcers, as well as for all types of peptic ulcer, acute or chronic, obstructive or non-obstructive.

[In the obstructive type when due to contracted scar tissue Sippy advises surgical treatment.—B.]

**Achylia Gastrica.** The technique used by E. C. Fishbaugh<sup>10</sup> of Los Angeles, in making a study of achylia gastrica, by the fractional method is described as follows:

The patient, in a fasting state, is given 40 grams of water crackers and 300 c.c. of water, as a test breakfast, about 50 c.c. of the water being reserved to be swallowed with the Rehfuß tube. The tube is swallowed immediately after the ingestion of the breakfast. The tube remains in the stomach during the entire period of the gastric digestion, and at intervals of twenty minutes from 15 to 20 c.c. of the contents are aspirated until the stomach is empty.

The specimen from each aspiration is filtered and the gross appearance as regards mucus and digestive changes noted. Measured quantities of the filtrate are titrated with one-hundredth normal sodium hydroxide, phenolphthalein being used as an indicator in the determination of the total acidity and dimethylamino-azobenzene for the free hydrochloric acid. Quantitative pepsin estimation is made by placing a Mettler tube into a mixture of equal parts of the anacid filtrate and tenth-normal hydrochloric acid, placed into an incubator, and the amount of digested albumin measured at the end of twenty-four hours. Qualitative rennin estimation is made by adding a few minims of the filtrate to 5 c.c. of fresh milk, allowing it to stand in an incubator for from 10 to 15 minutes, after which coagulation is noted.

The presence of rennin in the series of examinations has coincided with that of pepsin. In not a single instance was rennin lacking when peptic digestion occurred.

As a basis for this study, fifty-six cases have been selected in which carcinoma ventriculi or cancer of other visceral organs was definitely eliminated. Cases have been included, in which errors in diagnosis would have occurred, had the examination been concluded by an ordinary test breakfast removed within one hour after ingestion. The cases are grouped in three definite classes:

First, cases showing an absence of hydrochloric acid and enzymes,

(10) California State Jour. Med., March, 1919.

Second, cases showing an absence of hydrochloric acid with enzymes present.

Third, cases showing the presence of hydrochloric acid and enzymes, but appearing late in the digestive cycle.

Of fifty-six cases, only seventeen, or 30 per cent. belonged to the class in which there was an absence of both hydrochloric acid and the ferments, rennin and pepsin.

By the usual method of stomach examination, aspiration is necessary before the one-hour period, in order to secure a specimen of sufficient size for analysis, but in this series of true achylia, the emptying time varied from forty minutes to three hours, with an average of one hour and forty-three minutes. This average is somewhat more rapid emptying time than observed in normal individuals, but not so rapid as usually reported in achylia gastrica. It is doubtful if the stomach secretions ever return in this group of cases. Such cases as have been reported were not examined by the fractional method originally, and consequently the presence or absence of enzymes in the latter part of the digestive cycle was not known.

Twenty-two of the fifty-six cases, or 40 per cent., showed an absence of hydrochloric acid during the entire period of stomach digestion, but with pepsin and rennin present in normal or decreased amount.

The remaining sixteen cases of this series, or 30 per cent. showed a delay in the appearance of the hydrochloric acid for one hour or more, after which the acids and ferments were present.

In 75 per cent. of this group of patients the pepsin appeared early in the cycle of digestion, so that even though the one hour examination alone had been made, the pepsin would have been noted. But in four instances, the ferments were also delayed. In the first hour, the stomach secretions were completely absent, but in the second hour they became quite normal.

The emptying times in the spurious achylia present the greatest difficulties to correct diagnosis by the usual method of stomach examination, since they varied from one hour and forty minutes to three hours and thirty minutes, with an average of sixteen cases of two hours

and eight minutes—somewhat longer than observed in the preceding group.

Since 30 per cent. of this group could have been misdiagnosed by the one-hour examination, it seems evident that a more extensive examination is necessary in every case in which free hydrochloric acid is not found.

In conclusion, the author says that the fractional method, as above described, is exceedingly simple in technique, causes the minimum of discomfort to the patient, and affords maximum data in the least possible time.

All so-called achylia gastrica cases should be examined by the fractional method in order to group them properly.

The psychical achylia form a large percentage of cases which are easily misdiagnosed by the usual method of stomach examination.

The division of achylia gastrica cases into these four groups is of distinct prognostic and therapeutic value.

**Gastric Mucous Catarrh.** The term "catarrh," applied to gastric disorders is seldom used at present, writes L. Pron,<sup>1</sup> or rather whoever refers to "gastric catarrh," seems to mean generally continuous hypersecretion and nothing else. Now acid catarrh is merely a part of what may be called a gastric catarrhal state.

Every mucosa which has been diseased for some time, or subjected to violent irritation, shows a transient or chronic catarrh, the gastric mucosa as well as that of the nose, pharynx, etc. Even in stenosis of the pylorus, due to ulcer or cancer, the stagnation of food is accompanied by catarrh, which often overshadows the stenosis. As acid catarrh results from long-continued hyperactivity of the acid glands, so too, mucous<sup>2</sup> catarrh is the consequence of excessive and persistent functioning of the muciparous apparatus.

When there is splashing in the stomach, from twelve to fourteen hours after the last meal, and we are able to withdraw a thick fluid, which is alkaline, neutral, or slightly acid (with absence of free acid), we must conclude the patient has mucous catarrh.

(1) Archiv. d. mal. de l'app. digest., July, 1919.

(2) Synonyms: Gastromyorrhea; gastric myxorrhea; gastric mucorrhea, mucous gastritis; mucous gastrorrhea.

So far as identification of the gastric mucus is concerned, it seems strange that some believe saliva can be mistaken for it. The latter is full of air, floats and is distinct from the stomach contents no matter what these may be; it never mixes spontaneously, and can be separated in a test-tube.

Next to be considered is the esophageal mucus. Why should this be present in the gastric fluid? If we except cancer, and stricture due to syphilis or peripheral mechanical causes, the esophagus is an organ free from disease. Has catarrhal esophagitis ever been described, and if so why should gastropaths be affected. Here are two mucosae: first, that of the stomach which is completely healthy in but few persons, and which, in gastropaths, exhibits very frequently inflammatory or ulcerative lesions; second, that of the esophagus which apart from burns and the above-mentioned morbid conditions is very seldom affected. Why should it be supposed that the mucus found in the stomach comes from the esophagus?

Besides this theoretical reasoning we can appeal to the physical and chemical characteristics: The mucus from the esophagus is much more fluid and clear than that from the stomach; it passes readily through a filter; contains few chlorides, and does not exhibit the diversity of appearance seen in the gastric mucus.

The gastric mucus looks like a thick solution of gum; is viscid, (sometimes of glassy consistence so it can be drawn out, and flows scarcely at all), it filters either not at all or only with great difficulty, and as a rule contains many chlorides. The same sample may contain several varieties.

Pron states that he describes as gastric mucous catarrh those forms which are characterized by presence of fluid, abundant enough to set up splashing in the fasting stomach, neutral, alkaline or slightly acid, with absence of HCl, and containing no important element such as blood. A glairy fluid containing free acid signifies a catarrh above all acid—continuous hypersecretion. If markedly colored with bile it is biliary. When there is a notable amount of combined HCl, the acid factor domi-



nates for the diagnosis. The color varies, but is generally turbid, sometimes slightly yellowish.

Of the twenty-one examples studied by him, in eight the reaction was decidedly neutral, and the identity of these was undoubted. In three the biuret reaction (cold) was marked; in two slight, and wanting in three.

In six subjects, the reaction was feebly acid. In these early morning fluids, no other source than mucous catarrh could be assigned. In two the biuret reaction was clear, in two slight, in the others absent. The acidity was due once to the combined acid, in five to the acids of fermentation.

In the remainder (seven cases) the fluid was decidedly mucous, of a gummy consistence, and at the same time but slightly acid. Some six of them might be included in the class which Pron has called "incomplete acid catarrh." The biuret reaction was marked in three, medium in one and feeble in three.

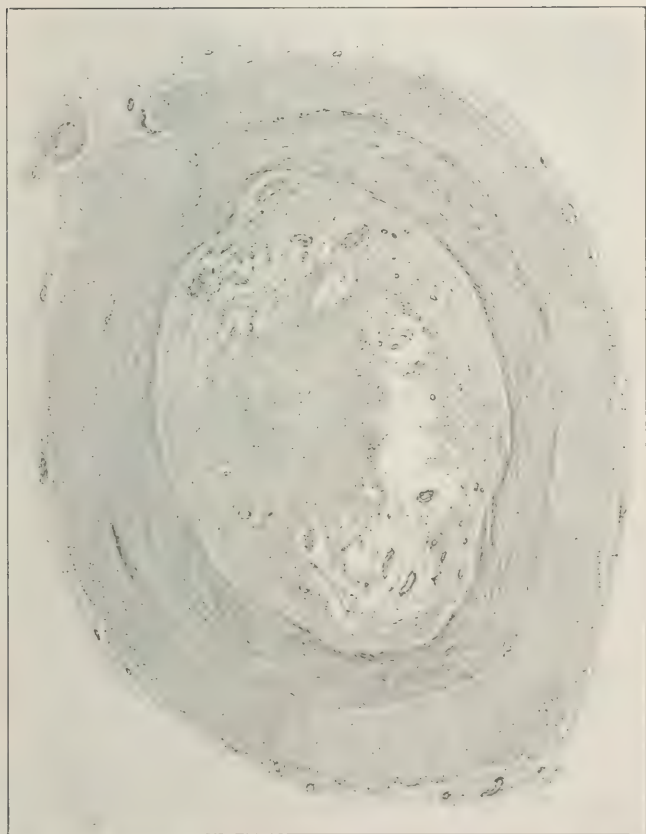
To seek for the causes of gastric mucorrhœa the etiology of the whole group of gastropathies must be studied. It has been attributed to alcoholism: this is erroneous. Alcoholic excesses do not lead to gastromyxorrhœa any more than ulcer or other morbid entity. All factors capable of disarranging the stomach either functionally or organically, directly or indirectly, may bring on this mucous catarrh. None of Pron's patients was an alcoholic.

The clinical picture can scarcely be drawn correctly, the symptoms vary with each case: Some individuals exhibit an apparently continuous hypersecretion with bulimia, regular pain, and total collapse while waiting for meals. Others seem to have hyperchlorhydria, with lessened appetite, and daily postprandial heaviness. Still others complain especially of colics early in the day, probably due to delay in passage of the thick mucus along the bowel. As a general rule, vomiting of mucus is very uncommon. Pron saw it in but four patients. As these symptoms are met with in all other gastric affections, there is nothing helpful about them.

The existence of mucous catarrh can only be determined without chance of error by passage of the stomach-tube in the fasting organ.

Objectively we note dilatation, an almost invariable

PLATE XVII.



Section of the appendix showing complete destruction of mucosa and obliteration of lumen by a mass of fatty and fibrous tissue.—Friedman, page 524.



accompaniment of every gastropathy of long standing: gastric atony evidenced by the late or early splashing: some disordered abdominal equilibrium usually affecting several organs; a nervous state, a common condition in dyspeptics; and rather often enterocolitis (seven times in the twenty-one cases).

Are we to see in such cases some secretory disorder developing simultaneously in stomach and colon, due to a single factor? Or, are we to look on the intestinal mucorrhœa as a consequence of that in the stomach?

Pron inclines to the latter, believing with Glénard and with Robin, that ordinary enterocolitis presents itself clinically as a symptom produced by disease of the stomach or liver, or both together, rather than as a definite morbid entity. Most often it improves very rapidly under treatment directed to the stomach or liver alone.

As far as treatment is concerned there is nothing to be done for the mixed mucorrhœa. This is a defensive reaction, the mucosa protecting itself against the irritation of the acid, hence measures must be directed against the hyperchlorhydria or the continuous hypersecretion.

In pure mucorrhœa, we should, theoretically, try to render the mucus soluble, by alkalies in the first place, *c. g.*, half a glass of warm *Vichy water*, in the morning fasting. Pron formerly used pure *carbonate of soda* 0.5 gm. in solution at the end of meals, with variable results.

In the diet, soft food such as purées, milk and fats should be avoided, these can only add to the mechanical effect of the excessive mucus. Substances should be chosen which exert some detergent action on the mucosa, *i. e.*, roast meat, green vegetables, rice, crust of bread well chewed, raw fruits. Salt and condiments also should be advised to start up contractility and favor emptying of the stomach, in the same way as do the gaseous mineral waters.

The symptomatology of the patient is to be taken into account, above all.

Meat is to be prohibited in patients with frequent pains; also spices and strong alkaline waters, taken cold. In such cases the diet must consist of fish, green

vegetables and eggs, with the common sage tea for evacuation of the glairy fluid. As for drugs, belladonna may be employed, it acts as sedative to the mucosa and possibly aids stomach peristalsis as claimed by Richaud. The following in soup-spoonful doses at the end of meals is a slight excitomotor:

Sulphate of soda, dry.....	
Phosphate of soda, dry.....	
Bromide of sodium .....	<i>a a</i> 3
Distilled water .....	300

Inversely in subjects who are at the same time hypoesthescic and hypochlorhydric, a meat, salt and spice diet may be advised but in moderation. We may resort to acid medication to fluidify the gastric mucus, either hydrochloric acid, 10 drops in half a glass of water at the beginning of meals, or phosphoric acid in the same dose. Tincture of nux vomica or something similar may be used as well to activate evacuation of the chyme.

In all cases, the ptosed organs must be supported by a belt correctly applied, and not placed too high, together with massage and hydrotherapy, cold or warm, according to the excitability of the nervous system.

**Bulimia.** While descriptions in text-books of bulimia are, as a rule, very good, the tendency to classify the condition with polyphagia in diabetes or exophthalmic goiter must raise doubt in the mind of any one who sees a case like the one reported by George Dock,<sup>3</sup> of St. Louis, or even one who reads a current definition, as to its place in pathology.

The patient upon the study of whose case this report is based was a man 36 years old. The complaint was that he had to eat more frequently and in larger quantities than normal. Hunger attacks would begin with a general feeling of uneasiness followed, if food were not taken, by an intense headache, generally in the eyes or frontal region. Sometimes headache came quickly if food was not taken. Sometimes it was delayed.

Family history and previous history were without particular significance in relation to the present trouble. The complaint of a voracious appetite dated from Janu-

(3) Amer. Jour. Med. Sci., March, 1919.



ary, 1915. At first, the patient felt hungry about 9 p. m. and would eat a bowl of rice or something similar. The condition gradually grew more severe. At the time of onset, he weighed 145 lbs.; when he was seen by Dock he weighed 215 lbs. He had recently grown short of breath. When the amount of food was large the bowels were loose. The patient was placed in a hospital and most thorough examinations of every kind were made. This report contains a record of complete physical examination, blood count, blood chemistry, urine examination, study of the spinal fluid, Wassermann reactions on the blood and spinal fluid, a study of the stomach content and stools, and extensive use of the *x*-ray.

The diagnosis made was as follows: Bulimia, pansinusitis, acute rhinitis, pharyngitis and laryngo-tracheitis, caries of teeth, and alveolar abscess.

The first night the patient was in the hospital, orders were left to give him anything he asked for. Between 8 p. m. and 6 a. m. he took 800 c.c. of milk, 5000 c.c. of water, ten shredded wheat biscuits, besides some bread cubes, total calories 1684.

During the next twenty-four hours he took calories 7038.

From exhaustive study it soon became clear that diabetes and organic stomach disease, intestinal disease, intestinal parasites and pancreatic disease could be ruled out. Pituitary disease and disease of the central nervous system seemed possible to exclude, also neurasthenia and hysteria.

The condition of the teeth and the nose and accessory cavities indicated something more than symptomatic treatment. The character of the food eaten between meals made one think of relief to reflex irritation, and the mouth and nose seemed possible sites of such irritation. It was advised that these local diseases be treated at once, with the hope that this might stop the chief symptoms. If not, further investigations into metabolism were agreed to by the patient.

In this study hunger contractions of the stomach could not be followed by placing balloons in the stomach as Carlson has done in his work. It seemed certain, however, from the Roentgen rays, as well as the clinical

observations that rapid emptying of the stomach had nothing to do with the hunger pains.

The patient was first seen by Dock early in February, and by May 1 his weight had been reduced from 215 to 185 lbs. He felt well and ate only three meals a day. The author states that it is perhaps going too far to assert that the treatment was the cause of the improvement. The fact remains, however, that following the clearing up of infections in the sinuses, the nose, and about the teeth, marked improvement in the patient's condition was observed. Many will think the condition was a neurosis, and the improvement a coincidence, perhaps only temporary, says Dock; however that may be, he considers the case a lesson in showing the advantage of treating local diseases that may cause functional disorder rather than resorting to the narcotic depressants or other symptomatic remedies still recommended and used in such cases.

The case illustrates another feature of therapeutics. For years medical teachers have emphasized the importance of treating the patient and not the disease, of ascertaining the complete anatomic and functional condition of the individual and correcting all anomalies. This would seem to mean that all morbid processes should be treated, instead of treating abstract conceptions.

Focal infections, sometimes causing local symptoms, always capable of setting up other and dangerous processes, would seem to indicate careful and exhaustive treatment, and yet there are seen all kinds of neuroses in patients with infections of the teeth, tonsils, prostate, or appendix, with but little or nothing done with the demonstrated foci unless a haphazard effort with vaccine.

**Value of Transitional Leukocytosis in Diagnosing Chronic Appendicitis.** The value of transitional leukocytosis in making a diagnosis of chronic appendicitis is discussed by G. A. Friedman,<sup>4</sup> of New York, who points out that while tenderness may be a point of much value in diagnosing acute appendicitis, it is not of great value in chronic cases, and does not always indicate true appendicular disease.

A hyperleukocytosis, or a polynuclear leukocytosis is

(4) Amer. Jour. Med. Sci., October, 1919.

also too often absent in chronic appendicitis. Routine examination of blood of so-called dyspeptics, many of whom were actually suffering from chronic appendicitis, suggests that in the differential count there is an important aid in the diagnosis of chronic appendicitis provided an enumeration of the large mononuclears and the transitional leukocytes be made. There is a definite increase in the number of these cells in the blood of persons suffering from chronic appendicitis, although this increase may be slight at times. It is found in chronic



Fig. 19. Showing the types of cells enumerated as large mononuclears and transitional leukocytes.

appendicitis more frequently than a hyperleukocytosis or a polynuclear leukocytosis and more often than the positive Roentgen sign. A transitional leukocytosis is absent in peptic ulcer, cholecystitis, renal colic, etc. If present in these or in other abdominal conditions, there is a chronic appendicitis complicating the existing conditions. The types of cells classified as mononuclear and transitional are indicated in Figure 19. Friedman considers that the percentage of transitional leukocytes in normal blood varies from 2 to 4 per cent., while the percentage of large mononuclears is 1 per cent. The total number of transitionals and large mononuclears in 100

white blood cells may therefore be considered as five, the absolute number of large mononuclears and transitionals in a normal white cell count of 10,000 per c.m. will be 400 transitionals and 100 large mononuclears. In other words, the transitional formula, sometimes called relative transitional formula, will be 5, and the absolute transitional formula 500.

An adequate explanation can not be given at present, says Friedman, for the extreme frequency of a transitional leukocytosis in chronic appendicitis. He suggests, however, that the transitional leukocytosis in chronic appendicitis is due to a constitutional disturbance, which may possibly also be disposed to appendicitis. The idea is strengthened by the fact that a hyperleukocytosis when present before an operation disappears after removal of the appendix, and the transitional leukocytosis often does not appear for months and even years after the appendectomy.

The basis of the present article is a study of sixty-five patients, and there are presented extensive tabulations of the blood count and clinical diagnosis in these patients. In Plate XVII there is shown the condition found in the chronically affected appendix removed from one of the patients of this group.

From this work, Friedman concludes that this case illustrates that the physical and Roentgen signs may be present without an actually diseased appendix, but the low transitional formula helped, indeed, to rule out appendicitis.

Transitional leukocytosis or an increase in large mononuclears and in transitional leukocytes or an increase in either of them, was found in the blood in 87 per cent. of patients in whom evidence of chronic appendicitis was obtained. There was no transitional leukocytosis in the blood of patients in whom evidence of chronic peptic ulcer was obtained or in the blood of those in whom cholecystitis, gall-stones or other organic abdominal conditions were found at operation. A transitional leukocytosis was found in patients in whom appendicitis was present, with other organic abdominal conditions. Hyperleukocytosis and polynuclear leukocytosis are not so frequently found in chronic appendicitis as transitional

leukocytosis. A transitional leukocytosis as a diagnostic aid is superior to such Roentgen signs as are supposed directly or indirectly to point to a diseased appendix.

**Diverticulum of Duodenum.** In his consideration of this subject, H. Siegrist<sup>5</sup> states it is rare; he was able to collect but seventy-three cases from the literature. His patient was a man, aged 48, who complained of gastric pain, anorexia and wasting. There was a history of abdominal trauma at the age of 13, following which there was acute pain in the umbilical region, with development of epigastric hernia soon after. Since that time, the painful crises had recurred at intervals; operation on the hernia had no effect. On palpation, a small swelling the size of a pigeon's egg could be detected to right of midline in the pyloric region. The x-ray showed at this point a round shadow close to that of the duodenum, which persisted even after the bismuth meal had passed by.

No exact diagnosis was made, but exploratory operation disclosed a cystic swelling, the size of a plum, which proved to be a diverticulum near the papilla of Vater, and adhering to the head of pancreas. Excision was easily done, and led to complete relief.

The contents were succus entericus without any foreign body. The structure was made up of the mucous tunic with numerous Lieberkühn glands, of the submucosa, and the muscularis mucosae with a few Brunner glands.

This was evidently an acquired diverticulum, more common than the congenital type, with a serous covering; moreover this last is more frequent in the first portion of the duodenum. Siegrist believes it is possible the trauma referred to may have wounded the pancreas, setting up partial atrophy of the head, and in turn giving rise to a *locus minoris*, which favored evagination of the duodenal mucosa. The painful crises may be explained by attacks of diverticulitis with retention, of which the adhesions were the reliefs. Radiography is important in such cases, it alone allows an exact diagnosis to be made.

(5) *Corr.-Bl. f. Schweiz. Aerzte*, Jan. 11, 1919.



## GASTRIC AND DUODENAL ULCER

**Diagnosis of Peptic Ulcer.** The object of this paper by J. B. Jackson,<sup>6</sup> of Kalamazoo, Michigan, is to review the records of eighty-two consecutive patients in whom the diagnosis of peptic ulcer was made, and to present what seemed to be the more important diagnostic features. The paper consists almost entirely of a detailed analysis of the symptoms and findings presented by these patients.

Of the eighty-two examined the diagnosis of gastric ulcer was made in fifteen, eleven of whom were males and four females. The diagnosis of duodenal ulcer was made in sixty-seven, fifty-two of whom were males and fifteen females.

Jackson states that the typical ulcer history is classical, the most constant symptom being pain in the epigastrium described as gnawing, burning or heavy, which is definitely related to eating, coming on from thirty minutes to three or four hours after eating. Patients with gastric ulcer usually complained of pain more promptly after eating than did those with duodenal ulcer. Many of these patients complained of pain at night, being awakened by pain at night when the stomach was empty. Some patients who have ulcer may complain of thoracic pain and some of pain in the lower abdominal region. Other prominent symptoms are nausea, vomiting and belching with regurgitation of sour fluid. Hematemesis and blood in the stools are further evidence in favor of ulcer. And it is often brought out in the history. Marked tendency to seasonal recurrence has been observed, especially in individuals with duodenal ulcer.

In the present work, twenty-nine patients with duodenal ulcer and five with gastric ulcer gave a history of being awakened at night by pain. Thirty-nine of those with duodenal ulcer gave a definite history of temporary relief from ingestion of food; while of those with gastric ulcer, ten gave a history of food relief. A definite history of relief from the taking of soda was obtained in thirty of the duodenal and in eight of the gastric cases.

---

(6) Jour. Mich. State Med. Soc., July, 1919.

In the entire eighty-two cases, a history of hematemesis was obtained in only four instances, two being duodenal and two gastric. A history of blood in the stools was obtained in eight of those with duodenal ulcer and in two with gastric ulcer, making a definite history of hemorrhage in 16.66 per cent. in the series. Vomiting was a pronounced symptom in nineteen of those with duodenal ulcer and in five with gastric ulcer. Previous to Jackson's examination, appendectomy had been done in nine of the patients with duodenal ulcer and in one with gastric ulcer.

The physical examination in cases of peptic ulcer is probably the least valuable of any of the means of diagnosis. The acute perforating cases give the clinical picture of peritonitis. Of the sixty-seven patients who had duodenal ulcer, forty-four had definite epigastric tenderness, and thirteen of the fifteen gastric ulcers had this sign. Thirty-four, or 41.4 per cent. of the group, had definite evidence of focal infection.

Concerning the laboratory findings, the author says that hyperacidity had been the rule in the analysis of stomach contents in patients with either gastric or duodenal ulcers. In doubtful cases, a marked hyperacidity might be determined. In this work the diagnosis of peptic ulcer in any case which showed a total lack of hydrochloric acid in the secretion was not made. Forty-nine of these patients were examined by the fractional aspiration method, and thirty-three by the single aspiration. The patients were not given a motor meal at night, so that no figures were obtained relative to the emptying time of the stomach, except such as were observed in *x-ray* examinations. All of the eighty-two patients were examined roentgenologically.

In analyzing the results of this method, Jackson says that of fifteen patients who had gastric ulcer, the niche was found in three. An accessory pocket did not occur. One patient was *x-rayed* following an operation for the repair of a perforation and the nichen sign which was undoubtedly present before the operation was replaced by a filling defect. Eleven of the patients who had gastric ulcer showed a massive six-hour residue. Two of these showed pyloric obstruction. Seven of the pa-

tients had an irregularity in the region of the pylorus, due either to spasm or to the collosity of the ulcer. There was one case of hour-glass stomach. Two cases showed a persistent incisura.

Constant definite duodenal cap deformity was observed in fifty-seven of the patients with duodenal ulcer. There was a marked gastric hyperperistalsis in sixty-one. Eighteen were observed to have the stomach empty at the end of two hours; unfortunately, not all the patients in this group were observed at this interval, so this number does not represent the total number of stomachs empty at the end of two hours. In eleven there was a definite gastric residue at the end of six hours. There was pyloric obstruction in five. Cap tenderness was observed in twenty-one of the sixty-seven patients.

In making use of the findings by *x*-ray examination, it is pointed out that the value of the ray in the diagnosis of abdominal disease can be estimated from the consideration of negative as well as positive findings. It is also pointed out that the patients studied in this work were sent to the author for diagnosis. None was under his immediate observation for either medical or surgical treatment. They came from many different sources. Of the eighty-two, seventeen were operated upon; ulcer was found in twelve of these. In one, diagnosed as probable gastric ulcer with obstruction at the pylorus, the surgeon reported that the ulcer was on the duodenal side of the pyloric ring. In another instance in which the diagnosis of both duodenal and gastric ulcer was made, the surgeon reported duodenal ulcer. In another instance in which the diagnosis was that of duodenal ulcer, the surgeon reported gastric ulcer. In one instance the operation was deferred and the patient died with symptoms of acute perforation, during the interval.

In five patients who were operated upon the surgeon reported that no ulcer could be found. One patient had a generalized peritoneal carcinomatosis. In two patients the only pathologic condition found at operation was chronic appendicitis and in one of these appendicitis had been diagnosed. In one patient who had a diagnosis

of duodenal ulcer, multiple cysts of the liver and right kidney were found at operation.

Concerning the findings of a surgeon under such conditions as these, Jackson remarks that except in large clinics, where many cases of ulcer are appearing for operation, the failure of the surgeon to find ulcer does not always indicate that the internist or roentgenologist is in error in diagnosing its presence. Of the patients in this group who were not operated on thirty-three have been reported remarkably improved under treatment by alkalis; fourteen are reported to continue to have symptoms of pain; seventeen of the patients had not been reported, not having been examined recently, or having been lost track of. Thus the non-operative cases in this group show a very gratifying result from medical treatment, judging from the reports which were available.

Granting that the diagnosis be correct, failure in medical treatment may indicate one or two things. It may mean that the ulcer is not amenable to medical treatment, or, what seems more likely, it may mean that treatment has not been thorough enough and sufficiently prolonged. This is often due to lack of coöperation on the part of the patient, but probably more often is due to lack of appreciation by the physician of the details of a thorough-going medical cure. Patients are willing to go to bed for a surgical cure, but rebel at such a procedure in medical treatment. To be successful, this treatment should be carried out with the patient in bed under absolute control for several weeks. The dose of alkali should be large enough to neutralize the acid of the stomach and keep it neutralized. This may be tested out by frequent aspirations. The dose of alkali as ordinarily given is altogether inadequate. The treatment must be carried out for several months in order to insure healing. Many of the medically treated cases recur because medical treatment is discontinued as soon as the symptoms are under control.

**Diagnosis of Gastroduodenal Ulcer.** In a lecture on this subject Anthony Bassler,<sup>7</sup> of New York, states that general practitioners diagnose correctly about 50

(7) New York Med. Jour., May 2, 1919.

per cent. of these ulcers. With some gastro-enterologists there is even a greater diversity than this.

He refers to some specialists who claim 100 per cent. correct diagnoses in the condition, and to others who make a correct diagnosis in none of the cases that come to them. A surgeon rarely makes a definite diagnosis, and when he does, he is wrong as many times as he is right. Finally, when the layman comes to the physician suspecting that he has an ulcer, he is always wrong. These statements are given to indicate how difficult it may be to make a correct diagnosis of the condition.

Concerning the history of such patients, Bassler says that the classical syndrome of duodenal ulcer, as expressed by Moynihan, is quite accurate and dependable. However, the characteristic three or four hour post-meal pain, relieved by eating or taking of alkalies, and the remission history, may be due to ulcer in the pyloric end of the stomach. The pain is variously described as burning, boring, lancinating, steady and dull in character, and generally localized in the epigastric region or at the costal edge of the left side. It may extend posteriorly and even radiate into the back and chest. It has relation to meals, their size and quality, coming on at once, or more or less late after them, the patient being less distressed when the stomach has been emptied for some hours. Lesser types of pain, more on the distress order, quite classical in relation to the time after meals, may be due to some gall-bladder condition or to marked status of gastric hyperacidity.

Another type of case that may closely simulate this syndrome in which cramps are the feature of the pain or distress, is that due to chronic appendicitis. There is a reflex gastrospasm, pyloric in location, or a true pylorospasm.

Hemorrhage is considered by Bassler to be classic in duodenal ulcer when it shows as a melena without vomiting in a case in which there is or has been the duodenal ulcer syndrome.

The posterior spinal tender area, first suggested by Boas, is frequently not found. Of the general symptoms less is to be said. Anemia, weakness and loss of weight are not constant, and may be produced by too many



other systemic conditions for any great importance to be attached to them in diagnosing ulcer. Nervousness, constipation, a little nausea, slight thirst, perhaps a degree of fever, a little leukocytosis, etc., is found in ulcer, but not oftener than in other conditions. Tenderness is mentioned first among the objective symptoms. This may be present in the epigastrium near the mid-line, and may be a factor in making a diagnosis, but other possible causes of such tenderness, such as gall-bladder disease and appendicitis, must be kept in mind when considering these.

In ulcer of the anterior wall, lesser curvature and duodenum, when the examination is made by a good roentgenologist, it may be most valuable in making or confirming a diagnosis.

The more indirect means of diagnosing ulcer by *x*-ray, namely tenderness on sharply localized pressure, and hypermotility in duodenal ulcer, have been discarded by the author. The *x*-ray diagnosis of gastro-duodenal ulcer is one of the most useful, and at the same time one of the most misleading means at the physician's command.

The factor rated as being of least importance in the diagnosis is such information as is obtainable from test-meal examination. When stomach contents have been carefully aspirated, the finding of importance is blood, next a high acidity, although these two are not conclusive, in fact, may not even be suggestive and of no importance. Where by test meal or *x*-ray method, or both, continuous secretion is diagnosed it points more definitely to ulcer than other conditions that may cause it, because in ulcer it is more definite.

Of the factors mentioned thus far, the history is most important, the *x*-ray next, physical facts next, and the laboratory last of all.

Of the complications of ulcer, perforation, when accompanied with hemorrhage is the most serious complication encountered. About 5 per cent. of all ulcers perforate, both gastric and duodenal perforations are more common in men than in women. Four out of every five perforations are single. Acute cases of perforated gastric ulcer or duodenal ulcer are easy of diagnosis, although no pathognomonic symptoms exist. The onset is

sudden, the pain and tenderness spontaneous, the pain spreading across the upper abdomen quickly. Deep breathing causes pain. This can be modified and patients assume the most comfortable attitude and complain of being moved. At first the abdomen is flat, tense and immobile, later, it distends but still remains tense and immobile. Collapse and prostration soon ensue, the temperature, at first stationary, rises or becomes subnormal. Perforation in subacute cases is characterized by a less marked onset. The features here are history of ulcer, change in character of pulse, distinct intensification of pain, the onset of abdominal wall rigidity, rise in temperature, and onset of leukocytosis with septic index. It is in cases of this type that diagnosis may not be made early. All patients with perforations should be operated on, subacute and chronic as well as the acute cases.

In the chronic case, definite diagnosis is rarely possible without the *x*-ray. There may be no local or general symptoms other than those due to ulcer. Those present are so vague that a diagnosis is not possible. As a rule these patients recover enough to get out of bed, and the extent of their complaining demands further examination in which the *x*-ray or the surgeon makes the diagnosis.

In the differential diagnosis of ulcer, one meets with such conditions as acute distress in the stomach due to indiscretion of diet, so-called gastralgia, cancer, hypersecretion, hemorrhagic and other forms of gastritis, pylorospasm, appendicitis, pregnancy with hyperemesis, uremia, gall-bladder pathology, kidney stones, epigastric hernia, arteriosclerosis, spinal-cord conditions, etc. By extensive work and process of elimination, the conversant have no difficulty in diagnosing any of the ulcers.

Most instances of perigastritis are due to other than ulcer conditions, but ulcer can bring about perigastric adhesions by causing inflammatory conditions of the peritoneum with resulting organization into adhesions.

In the early stage of ulcer, the onset of local irritative phenomena, retching, distress, dull pain, and possibly fever, should direct one's attention to peritoneal involvement. Adhesions may involve the gall-bladder or

the pancreas; in the first instance jaundice frequently results, and in the second a characteristic persistence and marked degree of backache is noted.

Cicatrices in the glandularis or the diffuse form in the stomach cases causing pyloric obstruction are easily diagnosable. There may or may not be history of ulcer, but there is always *x*-ray and test-meal stagnation beyond six hours, with the character of test-meal usually resorted to. Organic contraction is best diagnosed by the *x*-ray. Persistent excess of secretion can be taken as a post-ulcer condition, but is always due to dynamic interference with the passage of food and thus is a condensation acidity. Therefore a stagnant stomach is best diagnosed by mixed test-meals or the *x*-ray.

Chronic ulcer and the erosion of vessels are true sequels to the acute ulcer. If the cicatrix is large, in fact, if it is at all distinct and persistent, a corrosion of the margins or autodigestion of the central parts of the cicatrix may occur. The factors of importance here are the history of ulcer, small hemorrhages, errors in gastric secretion, gastric irritability, the intolerance to food, and colloquial symptoms of indigestion and more or less invalidism.

Concerning the so-called carcinomatous degeneration in ulcer, the author states that the majority of clinicians on the basis of so few ulcer cases ever becoming carcinomatous, think that the etiology and incidence are not at all proved. In his estimation about 5 per cent. of all ulcers become carcinomatous.

**Frequency of Diagnosis.** The diagnosis of gastric and duodenal ulcer is not made so frequently now as it was eight or ten, or even six years ago, says W. F. Cheney,<sup>8</sup> of San Francisco. He gives figures to show that in two groups of patients of about 450 each, one studied in 1912 and one in 1918, the number of diagnoses of ulcer, gastric or duodenal, in the first group, is about three times that in the second group.

The importance of history in making a diagnosis of these conditions is considered first in discussing the differential diagnosis of peptic ulcer. The well-known points in this history are its chronicity extending over

(8) Jour. Amer. Med. Ass'n, May 17, 1919.

years, its remission for weeks or months, during which the symptoms are absent or much less severe, its rhythmic cycle of events while an attack persists, the manifestations all relieved by taking food, but recurring at a variable interval after eating, and then increasing rapidly until food is taken again or some remedy such as soda, or until vomiting occurs. Finally, the patient's symptoms, such as heartburn, belching, water-brash, nausea, and often severe pain before vomiting gives relief. In general, there is complaint of acidity and sour stomach.

A history such as this one does not invariably mean ulcer, and also ulcer may exist even though the history does not correspond with the usual type. To infer ulcer from history alone frequently leads to error; also ulcer may exist without hyperacidity, with normal or subnormal acid values. A history of vomiting blood is not a common incident, and is not common with ulcer; and on the other hand, it is a well-known fact that hematemesis may occur in association with hyperchlorhydria from any cause when no ulcer exists.

The usual, physical examination of patients who have gastric or duodenal ulcers reveals little or no gross abnormality. Palpable tumors in the abdomen are more likely to be neoplasms. The discovery of a peristaltic wave across the stomach from left to right, usually means pyloric obstruction and hypertrophy of the gastric walls. But it does not by itself indicate ulcer. Other intra-abdominal conditions, such as obliterative appendicitis or gastropotosis, may present a similar absence of physical signs, with an exactly similar ulcer history. *Tuberculosis dorsalis* presents entirely negative findings over the abdomen on physical examination.

Less emphasis is placed on the results of an analysis of gastric content now than has been done formerly. Ulcer is most often associated with hyperchlorhydria but, on the other hand, hyperacidity may be associated with numerous other conditions besides ulcer.

Concerning the value of fluoroscopy and roentgenoscopy, Cheney says that in no case of suspected ulcer should a conclusion be reached without the aid of these measures. The information thus obtained about the

PLATE XVIII.



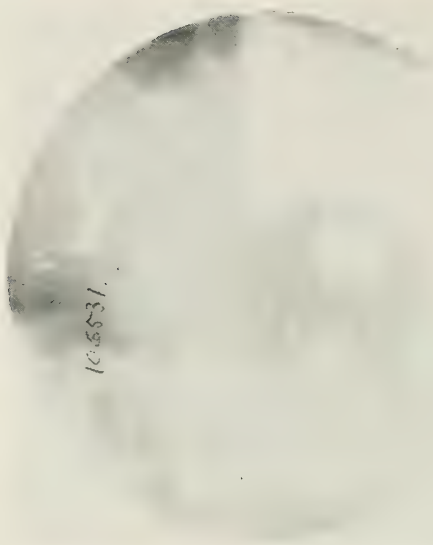
Niche of gastric ulcer. Carman, page 539.



PLATE XIX.



A. Perforating gastric ulcer without accessory pocket formation.



B. Large gastric ulcer. Microscopic examination showed malignancy. — Carman, page 539.

outlines of the stomach, of the duodenal cap, the rate of peristalsis and the emptying time of the stomach, adds demonstration to inference, and either confirms or disproves the suspicion aroused by history, physical examination and analysis of stomach contents. It has been learned that if no evidence of ulcer appears from the roentgenographic examination, that one must distrust all other evidence, no matter how convincing it appears.

On the other hand, apparent defects in the outlines of the pylorus or the duodenal cap, suggesting the presence of ulcer, should not be interpreted as positive proof unless other evidence co-exists in history and stomach analysis. The person who makes *x-ray* examinations must be willing to repeat examinations, confirm dubious results, and not be too ready to furnish a diagnosis from his findings alone. What the clinician wants is roentgenographic evidence, not roentgenographic diagnosis.

Among other conditions producing symptoms resembling ulcers, Cheney mentions chronic appendicitis first, because it often leads to a history that is typical of ulcer, and to reflex pyloric spasm, which results in hyperchlorhydria. Careful study, however, should lead to a correct diagnosis, and he says that there is no excuse for the old error so frequently made of an operation for ulcer resulting in the discovery of no ulcer present, followed by a second incision over the appendix for its removal.

The clinical history of a patient with chronic cholecystitis is frequently persistently made up of the symptoms characteristic of ulcer, and the physician may be misled by it. In this condition, however, sharp paroxysms of colic, with transient jaundice, are usually mentioned. Physical examination soon after one of the exacerbations of a chronic gall-bladder inflammation may reveal much tenderness and definite muscle spasm at the right costal margin with increased fullness and tension there. The stomach analysis shows hyperchlorhydria, but nothing to indicate either ulcer or gall-bladder disease as a cause. Roentgenographic examination eliminates evidence of gastric or duodenal ulcer.

Gastroptosis enters considerably into this differential diagnosis. The author states that there is undoubtedly one large group of gastroptosis cases that closely re-

sembles ulcer. This is because of the hyperchlorhydria which results from faulty position. Here also roentgenographic evidence excludes ulcer and demonstrates gastropptosis more definitely than any other method can. While there are differences of opinion as to how low in the abdomen the stomach may normally be found, there seems to be agreement that a greater curvature lying below the level of the iliac crests constitutes an undoubted abnormality.

In gastric cancer it is usually found that the history in this condition is entirely different from that in ulcer—as regards a shorter duration of symptoms, their persistence without intermission and their character. But not infrequently cancer occurs on an ulcer base, and the history then becomes confusing and no longer characteristic. Symptoms may have persisted for years with intervals of comparative good health between attacks, and the details of these former symptoms may correspond in every respect to those of ulcer. But when cancer develops the story is of a change in the manifestations: the pain becomes more constant; food is not desired; soda and other remedies, as well as food itself, no longer give relief; taking food causes distress at once, with no interval of comfort following, and the patient loses in weight and color, as in no previous ulcer attack. Physical examination may now show definitely a tumor in the upper abdomen. Its presence, as already stated, is always to be looked on with suspicion, though its absence does not exclude cancer, because it may be concealed and out of reach.

When cancer is present, there is usually a complete absence or a great decrease of free hydrochloric acid. Whether or not a palpable tumor has been found, the roentgenograms will show its presence or absence, and its site, if present. In making the diagnosis, however, the data elicited by history, physical examination, and gastric analysis must all be taken into account, as well as the roentgenographic findings.

Other intra-abdominal pathologic considerations that are mentioned by Cheney are intestinal parasites, especially tape worms, small hernia due to defects in the abdominal wall around the umbilicus, or along the linea

alba. One must also take into consideration the absence of other physical signs, and the negative findings in roentgenograms, in deciding that there is not other cause for the history given, such as chronic pelvic inflammatory disease in women, and old adhesions involving intestinal walls in a former peritonitis, or other conditions that at times may simulate ulcer in the way described above.

The hardest lesson to learn about abdominal disease is that of "gastric crises," due to no disease within the abdomen itself, but to disease in the spinal cord. These crises come at irregular intervals, weeks or months apart, with good health between. They last for days or weeks, and the attacks are characterized by intense pain and by vomiting, so that the patient fears to take food and can not keep it if he does.

Negative findings and other definite signs now point out the real disease.

Gastric neuroses are still mentioned in the text-books, in the differential diagnosis of ulcer, but their existence outside of text-books must be considered very dubious.

**The Roentgen Diagnosis of Gastric Ulcer.** As a preliminary to considering factors that are actually demonstrated by means of the *x*-ray in this work, R. D. Carman,<sup>9</sup> calls attention to the fact that a knowledge of normal conditions as revealed by the *x*-ray is essential to a proper understanding of abnormal conditions. Stomachs that are markedly dissimilar in their roentgenologic characteristics may each be appropriate for its possessor and may functionate in a normal manner.

In ascertaining whether or not a given stomach is normal, account must be taken of its length, breadth, capacity, contours, position forms, tonus, mobility, peristalsis and motility. These are also modified by the physique or body form of the individual. Any stomach that does not correspond to the body form should be looked upon with suspicion.

In the routine Roentgen examination of the gastro-intestinal tract, three varieties of stomachs are encountered: the normal, the reflex, and the pathologic. The distinction of the pathologic and the reflex is often trou-

(9) Journal-Lancet, Aug. 1, 1919.

blesome. The reflex manifestations which are commonly of a spasmodic character occur frequently in association with disease of the gall-bladder or appendix, and occasionally in neurasthenia, tabes, intoxication, renal calculus, and other conditions. They produce the most numerous and the most deceptive counterfeits of pathologic signs; their careful exclusion is always essential.

From the statistics accumulated in Carman's work at the Mayo Clinic, he considers that nine-tenths of the ulcers of the stomach give distinct roentgenologic indications of gastric disease.

As seen at operation four types of gastric ulcer are distinguished: (1) Small, exceedingly shallow mucous erosions; (2) penetrating or callous ulcers with relatively deep craters; (3) perforating ulcers with or without the production of an accessory cavity; (4) carcinomatous ulcers, perforating and non-perforating.

Small shallow ulcers are mere erosions, and unless accompanied by secondary Roentgen signs such as the incisura or the incisura in combination with a six-hour retention, their presence is not likely to be suspected.

The penetrating ulcers, which have burrowed more or less deeply into the gastric walls, produce a definite crater jutting out from the lumen of the stomach.

Perforation of an ulcer with a continuation of the destructive process into adjacent tissues results in the formation of an accessory cavity outside of the stomach.

Early carcinomatous ulcers are not distinguished, as a rule, from non-malignant ulcers. Their roentgenologic signs are the same as those of penetrating or perforating ulcers.

The Roentgen signs of gastric ulcers may be described as follows: The niche, the accessory pocket, the hour-glass stomach, organic, spasmodic.

For convenience, the application of the term "niche" is limited to the visualized crater of a penetrating ulcer, the cavity of which lies entirely in the walls of the stomach. The niche shows as a bud-like prominence on the peripheral outline of the stomach, as shown in Plate XVIII. The clearness with which a niche may be seen depends on its location and whether or not the stomach can be seen at a proper angle. A small niche



in any situation may be hidden or partially obliterated when the stomach is distended, so that careful observation should be made while the stomach is being filled, especially when the patient is drinking the aqueous mixture.

An accessory pocket is apt to perforate against or into the liver, or to invade the pancreas. When visualized by the barium meal, the contents of the pocket are stratified like those of the stomach; the opaque barium at the bottom has a translucent layer of fluid above it, and this in turn is capped by a small gas bubble.

A six-hour rest in the stomach is often associated with perforating ulcers, whether or not they form accessory pockets. Organic hour-glass stomachs sometimes accompany an accessory cavity (Plate XIX).

The hour-glass stomach is next considered. In this type the construction is due to permanent structural changes in or about the gastric walls. The stenosis thus produced is often increased by spasm of the circular muscle fibers, but regardless of this fact, the condition is essentially organic and stable. The indentation of the greater curvature is, as a rule, relatively narrow and results in a correspondingly short isthmus along the lesser curvature, which gives the deformed stomach the semblance to the capital letter B. This serves generally to distinguish it from the cancer hour-glass stomach which usually is of an X-shape, with a rather long irregular canal, centrally placed. Roentgenologically it can not be differentiated from the spastic type of hour-glass stomach resulting from ulcer.

All forms of organic hour-glass stomach have certain features in common: They are not relaxed by general narcosis and are constant in situation; they can not be effaced by epigastric massage; and they remain unaltered after the patient has been given atropine or belladonna to physiologic effect.

Of the spasmodic hour-glass stomach, the incisura, there are two types, the intrinsic and the extrinsic. The most common cause of the intrinsic is gastric ulcer. The extrinsic is due to reflex spasm arising from sources outside the stomach and may exactly stimulate the hour-glass of ulcer.

The common features of extrinsic hour-glass stomach are as follows: It may change in appearance during examination; it is relaxed by a general narcosis; it may sometimes be erased by steady, forceful, though not violent epigastric massage; it is often absent at a second examination; and it disappears after the giving of an antispasmodic to physiologic effect.

A distinct residue in the stomach from the six-hour meal, amounting to a quarter or more of the quantity taken, is a relatively common accompaniment of the various types of gastric ulcer. Taken alone it would not support a diagnostic opinion.

Concerning carcinomatous ulcer, the author states that in a general way ulcers always project from the gastric contour, while in carcinoma the growth with its resultant irregularity extends into the gastric lumen. Between the typical ulcer and the typical carcinoma there is a small percentage of cases in which the roentgenologic differentiation is impossible. These are the border-line cases, in which carcinoma cells are found in the ulcer. In such instances the *x*-ray signs are chiefly those of ulcer, and a diagnosis of ulcer is likely to be made.

The differentiation of pyloric ulcer from pyloric cancer is sometimes very difficult. The roentgenologist can only say with certainty that a lesion exists. A correlation of his findings with the clinical data may justify an opinion that one or the other condition is present.

The diagnosis of gastric ulcer is then most important because of the fact that an ulcer sometimes shows carcinoma cells, and its diagnosis, in many instances, is equivalent to an early diagnosis of cancer.

Whether the malignant ulcers of the stomach start as malignant ulcers or change from benign ulcer to cancer, no one knows. Consequently, the medical treatment of gastric ulcer on the one hand and procrastination against surgery by physician and patient on the other, may occasionally deprive the patient of the only chance for cure.

**Ulcer and Ptois of Duodenum.** Durrieux and Par-turier<sup>10</sup> give the details of a case of ulcer of the second

(10) Prog. méd., Nov. 22, 1919.

portion of the duodenum, with intense and permanent vertigo. The diagnosis and localization, verified by operation, were established in spite of ptosis by means of the following signs to which the authors attribute great importance:

1. A painful point located in the middle of a line running from the umbilicus to the 10th rib, 6 cm. from the umbilicus and 5 cm. from the midline. This was constant in all positions and not influenced by respiration, provided the palpation was progressive, deep, and perpendicular to the axis of body.

2. Painful point in left cervical region obtained by pressure between the two heads of the sternocleidomastoid muscle.

3. Elective action of belladonna on the duodenal pain, opium being particularly efficacious in affections of the bile passages.

**The Diagnosis and Treatment of Chronic Gastric Ulcer.** This excellent paper was read at the opening session of the Harvey Society Oct. 23, 1919, by Sir Berkeley Moynihan,<sup>1</sup> surgeon to the Leeds General Infirmary.

A brief discussion of the anatomy of the stomach is presented first. It is pointed out that an ulcer occurring on the proximal side of the pyloric vein is designated as a gastric ulcer. One occurring one-quarter of an inch or one-half an inch or more beyond it is a duodenal ulcer. It is not merely a matter of academic interest to distinguish them. Their symptoms are sufficiently distinct to allow an accurate diagnosis of duodenal ulcer which may be made with remarkable constancy; their complications and sequels in respect to perforation and hemorrhage are very different. Cancer develops often upon the base of the gastric ulcer, and almost never upon the base of an ulcer in the duodenum. Gastric ulcer is a disease of comparative rarity: its diagnosis from the clinical evidence alone is difficult. Its mimicry by other conditions is extremely frequent.

Moynihan contends that full clear and truthful descriptions of the symptoms of gastric ulcer are rarely given, and that the conditions described as gastric ulcer are in the majority of cases indicative of other disease.

---

(1) Brit. Med. Jour., Dec. 13, 1919.

Concerning the symptoms of this condition he says that ulcer of the stomach occurs twice as often in men as in women, and its chief symptom is pain. In all cases of gastric ulcer there are periods of intermission during which there are no symptoms, but when the attacks are present, pain is the chief feature and its most constant attribute is the regularity that it displays. The interval between the taking of the meal and the onset of pain is fairly constant. As a rule the earlier the pain is felt after a meal, the nearer the ulcer is to the esophagus. If pain comes two, three or four hours after a meal, the ulcer lies generally beyond the pylorus. This period of relief from pain after a meal is constant and invariable, both in gastric and duodenal ulcers, until stenosis, subacute perforation, or the formation of crippling and embarrassing adhesions takes place.

The pain in cases of gastric ulcer very often disappears after an hour, or even less, and may be completely relieved, indeed it generally is, before the next meal is due. The pain of duodenal ulcer, on the other hand, appearing later, generally persists, often with a slowly increasing severity until the meal is taken. The character of the meal influences the pain. A generous meal of heavy foods causes severe pain to appear at an earlier time in gastric ulcer, it delays the appearance of pain in a duodenal ulcer.

A bland and blameless diet taken in small quantities at brief intervals may reduce the chances of pain appearing or even afford complete relief. Pain in the majority of cases is said to be on the left side or high in the epigastrium; in some severe types there may be complaint of pain in the back. It is noted that many patients attacked with acute pancreatitis suffer most from pain in the back, and a deep erosive ulcer of the stomach may also produce the same symptoms. The position of the ulcer, its freedom from adhesions from neighboring parts and its size, all seem to affect the type of pain, its period of latency and its time of onset after a meal. When ulcers are small and seated high up on the lesser curvature, or just on the posterior surface, the symptoms are shorter in duration but more prone to return. If the ulcer is large, excavating the liver, or burrowing deeply

into the pancreas, or if it is fixed by firm broad adhesions to the abdominal wall or the liver, the symptoms are less likely to show those intermissions which are so characteristic of the earlier stages.

About one-fifth of the patients who are found to have gastric ulcers complain not only of pain, but of great prostration, feebleness or lassitude, coming on just at the time when the pain is due. On close inquiry this most distressing symptom may be found to have preceded the experience of pain by weeks or months. The periodicity of the two is identical.

It is not possible to emphasize unduly the importance of ascertaining all these various modifications of the one symptom pain. The constancy of the sequence—food, comfort, pain; food, comfort, pain—is the most important of all the clinical matters concerned with the diagnosis of gastric ulcer. In all forms of ulceration of the stomach, or duodenum, vomiting is an inconspicuous feature, unless obstruction has developed as the result of the cicatrization of the ulcer. In the earlier stages of the development of the malady, vomiting is not seldom self-induced in order to ease the stomach of the heavy load and a sense of pressure and oppression. A very little experience seems to teach the greater number of patients the quantity of food that is appropriate for them. Thereafter, vomiting occurs quite infrequently.

When there is frequent vomiting, with inability of the stomach to tolerate the presence of any food, even fluid nourishment sparsely taken being at once rejected, gastric ulcer as the cause should be driven from one's mind.

In the case of ulcer, the meal at first causes relief, and only after that period of relief does it cause disturbance.

Hematemesis also occurs far less commonly than is generally supposed. That gastric hemorrhage occurs profusely in ulceration, both of the stomach and the duodenum, is certain, but the number of other conditions that give rise to hemorrhage is so large that the possibility of the gastric ulcer being the source of the blood should not be strongly or exclusively held. If the



breaches of continuity, which permit the escape of blood in cases of cirrhosis of the liver, splenic anemia and the toxic conditions which as a rule have their origin within the abdomen are called acute ulcers, as they often are, it is essential to remember that such ulcers are recognizable by no other clinical evidence than hemorrhage, or in exceedingly rare instances by perforation. They are never the cause of continuing or recent dyspepsia.

It is emphasized that the possibility of making an accurate diagnosis of gastric ulcer is greatly increased by the x-ray examination, that indeed, the radiographic examination alone is more accurate than all other methods combined; and that a diagnosis that is proved by subsequent operation to be correct in indicating the presence of ulcer, or in demonstrating its size, and position, can be made in about 90 per cent. of the cases.

The radiographic signs of gastric ulcer are recited as follows: The direct evidence consists of a demonstration of the ulcer cavity itself. If the ulcer is near the lesser curvature, it is visible in either an anterior or posterior or semi-lateral view. If the ulcer is on the posterior surface the best view is obtained when the stomach is empty. An ulcer on the anterior or posterior surface of the stomach, close to the pylorus, is more difficult to demonstrate. Considering indirect evidence, Moynihan says that in the majority of cases of gastric ulcer, a very remarkable and sustained contraction of the circular muscles of the fibers of the stomach occurs in or near the segment in which the ulcer lies. An indentation of the greater curvature of varying degree and extent, but often so considerable as to appear almost to bisect the stomach, is most clearly seen. Its appearance whether on the screen or on a photographic plate is remarkable. The spasm in a majority of cases remains stationary during the examination. It is unaltered, by palpation, massage, or by the administration of large quantities of belladonna. It relaxes under general anesthesia, and is not seen on the operating table, the stomach wall being then quite soft and flaccid.

The presence of the persistent spasm is strong presumptive evidence of the existence of an ulcer. The

presence of an incisura on the greater curvature, with a bud-like opaque projection on the lesser curvature is an unequivocal evidence; in every such case an ulcer is present.

Of the chemical examination of the stomach content, the author does not speak with any enthusiasm. He can not think that the evidence thereby obtained enables a greater accuracy to attach to the diagnosis or justifies the increased trouble that it gives to the patient. In rather over 40 per cent. of the total number of cases in which an ulcer is present, there is no hyperchlorhydria, and in a small number, estimated at from 10 to 20 per cent. there is a reduction in the gastric acidity.

Physical examination in the absence of obstruction in the body, or at the outlet of the stomach, reveals very little in the matter of diagnosis of the gastric ulcer.

In considering differential diagnosis, he states that the great difficulties in the diagnosis of gastric ulcer are due to reasons which can not now be fully appreciated. An ulcer of the stomach does not arouse symptoms merely because of the gap in one or more of the several layers of the stomach. One may be certain of this cause after an attack of gastric ulcer is over, and the patient is wholly free from symptoms. An operation may disclose an open crater of an ulcer large or small. The exact cause of the symptom is uncertain, but so far as is known at present, other conditions in addition to the structural defects ~~must~~ be present before the symptoms appear. These are: First, evidence of infection around the ulcer, such as induration, local peritonitis, the deposit of fat in and around the base of the ulcer, and enlargement of neighboring glands; the sentinal gland of Lund is constant in cases of active ulceration.

Second, spasm of the musculature of the stomach may contribute to the symptoms present.

Third, an increase in the acidity of the gastric juice. The hyperacidity is by no means constant, either in gastric or in duodenal ulcers, but it is possibly a factor of importance in the awakening of symptoms.

The author's own strong feeling is that in order to

obtain precision where so much has been vague, no diagnosis of chronic ulcer should now be confidently accepted unless the ulcer is diagnosed by *x*-ray examination, or displayed on the operation table.

Under the heading of treatment of chronic gastric ulcer, medical treatment is first considered.

Here, hope is expressed that there may now be agreement that the results of the treatment of gastric ulcer by any of the systems mentioned, or by any dietary or medicinal regime, are vitiated by the lack of accuracy in the diagnosis of gastric ulcer.

He says that the most rational of all methods is that introduced by Sippy, which would appear to meet more competently those conditions in the stomach which it is believed must be controlled before an ulcer has a chance to heal. It is based on a recognition of the fact that the reduction of the acid in the stomach is the first step. This is obtained by a dilution of food, alkalination of the gastric content every hour, and by the administration of fats.

The questions which in this connection require answer, are:

1. Does a chronic gastric ulcer ever heal under medical treatment?
2. Does it long remain healed?
3. Does it heal without producing such conditions as need surgical treatment for their relief?

Concerning the first question, Moynihan states that chronic gastric ulcer undoubtedly heals under treatment, or after the exercise of continued care in diet. As to the second question, in the majority of cases, the answer must be no. The characteristic quality in the symptoms of gastric ulcer is recurrence.

In answer to the third question, he states that when a gastric ulcer of moderate or large size heals, there is inevitably some degree of contraction. In this way hour-glass stomachs are produced, and stenosis near to the pylorus.

Under the heading of surgical treatment, Moynihan says that when a chronic gastric ulcer has refused to heal, or has recurred after medical treatment, surgical treatment is necessary. There is not yet any close agree-

ment as to the procedure which is best adapted to the various types of cases, and there is not yet available a full record of the after-history of large groups of cases.

The operation of gastro-enterostomy is that which has been most frequent in practice. It may be supposed to have two effects, a mechanical one, whereby the stomach is more readily drained and a physiologic one, as the result of which the gastric contents are alkalized by the escape into the stomach of the pancreatic juice and the bile. The author is personally averse to the performance of gastro-enterostomy except in cases of existing or threatened obstruction—that is in cases of duodenal ulcer or in special circumstances only of prepyloric ulcer. The whole matter requires fuller investigation. The effect on the healing of the ulcer and on the spasm of the stomach as judged by the *x*-ray must be studied and the result of operation carefully recorded.

He feels that in the majority of gastric ulcers it is better to perform partial gastrectomy. That appears to him to be the only way to make sure of curing the patient. The advantages of gastrectomy over all other operations is that it does away, so far as the author's experience goes, with any chance of recurrence of the ulcer, that it results in a complete and immediate freedom of all gastric troubles, and that it banishes the danger—it may be large or small, but it certainly is real—of a cancerous change taking place in the base of the chronic ulcer. In the last forty specimens removed on account of simple gastric ulcerations by the author, three showed early evidence of carcinoma. It is true that in a majority of cases an active discrimination between simple and malignant ulcers may be made. But no one is competent always to judge it rightly, and it is safer to decide by microscopic examination in a captured specimen than to learn of a mistake by a late issue of the case.

**Medical Treatment of Gastric Ulcer.** The first and one of the most important factors in the successful treatment of gastric ulcer is absolute rest in bed for a period of at least three weeks.

The purpose of medical treatment is to produce conditions in which the stomach contents are neutral or alkaline in reaction, in order to remove the irritation.

The author of this article, Owen King,<sup>2</sup> states that he has used the treatment as outlined by B. W. Sippy of Chicago, and has had uniformly good results.

The treatment as outlined here is as follows:

At 7 a. m. the patient is given a powder (No. 1) containing 10 grains of calcined magnesia and 30 grains of sodium bicarbonate; at 7:30 a. m. an ounce and a half of milk and an ounce and a half of cream; at 8 a. m., a powder (No. 2), containing 10 grains of bismuth subnitrate and 30 grains of sodium bicarbonate. This treatment is followed during the day, the powders being given on the hours and the milk and cream on the half hours up until 8:30 p. m. At 9 p. m. the stomach contents are aspirated carefully, and sent to the laboratory for examination which includes an examination for occult blood and the determination of the free and combined HCl. The combined HCl causes no symptoms and probably does not cause much erosion. If the examination shows an absence of free HCl the same-sized powders are given the following day which were used on the previous day. If on the other hand, free HCl is present, the sodium bicarbonate is increased 10 grains in each powder, and the same routine is carried out for the next day. At nine o'clock on the second night and on each night afterward, the stomach is aspirated and an analysis made. In this way we can determine whether or not we are controlling the HCl, thus removing its irritative action on the ulcer. It is very gratifying, indeed, in cases which on the first few days present marked symptoms of obstruction to see the amount of retention gradually decrease until in a few days the nine o'clock aspiration will give a normal amount of stomach contents. In the author's experience, there have been one or two cases which, when aspirated at nine o'clock, showed an almost complete pyloric obstruction—that is, as many and usually more ounces of liquid would be obtained than were given during the day. After a few days of treatment the amount aspirated gradually decreased to normal.

About the third day, an egg is given and on the fourth day an egg and a cereal. Each day following the diet is increased by the addition of an egg or a cereal until two

(2) *Journal-Lancet*, Dec. 15, 1919.



weeks have passed. Usually by this time there is no retention, and the free HCl has been controlled for some time. If at any time during the night the patient complains of irritation, burning, or pain in the stomach, it is aspirated and the contents sent to the laboratory for examination. Occasionally, cases are found which seem to have a hypersecretion at night, and it may be necessary to control this by administering a few powders at irregular intervals. The patient is soon taught to aspirate his stomach himself, and, usually at the end of a week, he can do it with less discomfort than if aspirated by a nurse.

Cases of bleeding ulcer will show the presence of blood, usually, only a few days when under this treatment. It is generally necessary to examine the stools for occult blood, for, if the ulcer is on the duodenal side of the pylorus, we will not obtain the blood in the stomach contents.

Patients soon learn to use the indicator, and, if they find free acid is present, they increase the size of the powder for the next day or two. The length of time that they are under observation depends on the severity of the case and the results of treatment. All patients who have any evidence of focal infection, arising from bad tonsils, teeth, or infected sinuses, should have these things corrected before treatment is started. There is no doubt that some patients who have been under medical management for gastric ulcer will return in a year or two with a recurrence or a new ulcer. The question then arises: Is this a recurrence of the old ulcer or has a new one developed due to some causes which have been overlooked or undetermined. The author is satisfied that very few patients who have followed this medical treatment in detail will have a recurrence. The results, as a whole, will certainly be more satisfactory than with surgical treatment, for the principle of surgical treatment when a gastro-enterostomy is performed is to produce a rapid emptying of the stomach. The author believes that every case that has been treated surgically should be followed by an appropriate medical treatment in order to give the ulcer every opportunity to heal. In cases in which gastro-enterostomy has been done, the *x-ray*, shows

that the artificial opening is used only so long as there is obstruction to the pylorus, either of an anatomic or a spasmodic nature. As soon as the pylorus can functionate normally, most of the food passes through that outlet.

It is not contended that every case of peptic ulcer will respond to medical treatment. There are, no doubt, cases of marked pyloric obstruction from old scar tissue of healed ulcers, and stomachs that will not empty after the spasmodic feature of the pylorus has been eliminated, which must have surgical treatment. There is an actual mortality of from 3.5 to 4 per cent. in gastro-enterostomy under the best surgeons, and 10 per cent. mortality with the average surgeon, while with the medical treatment there is practically no mortality.

King does not advocate stubborn persistence in medical treatment in cases in which one observes no response, or in cases in which one finds the patients losing ground. No one can doubt that the great majority of ulcer cases are curable by properly applied medical treatment. In discussing and comparing surgical and medical treatment the question should not be whether to prefer one or the other on general principles. Each has its field, and each has its justifications and limitations. Personally, the author has become convinced that the many failures of medical treatment must be attributed to superficial application of proper medical management during an insufficient period of time and a failure to recognize the principles on which a cure is based.

**Duodenal Alimentation in Peptic Ulcers.** Results obtained by the treatment of peptic ulcer with the duodenal alimentation, are published by Max Einhorn.<sup>3</sup>

He divides peptic ulcers into the following groups: (1) Uncomplicated cases of moderate duration; (2) uncomplicated cases of long duration; (3) cases complicated by recurrent hemorrhages; (4) cases complicated by obstruction of the pylorus; (5) cases complicated by perigastric adhesions or perigastritis.

All uncomplicated cases (Groups 1 and 2) are amenable to medical treatment, especially to duodenal alimentation. Group 3 should be given a trial by duodenal ali-

(3) Med. Record, July 19, 1919.

mentation. If hemorrhage returns pretty soon after this mode of treatment, an interval operation (gastro-enterostomy, sometimes, with pyloric occlusion) should be performed. Groups 4 and 5 usually require surgical measures. However, if the stenosis of the pylorus has not reached a high degree, medical treatment can first be tried and, if necessary, be followed by stretching of the pylorus through the internal route.\* In perigastritis, the rest period during duodenal alimentation brings sufficient relief to forestall an operation.

The results of duodenal alimentation in peptic ulcer will depend to a great extent, first, on the proper selection of cases, and on a correct diagnosis; second, on a conscientious and detailed handling of this mode of treatment.

The author has treated in all 315 patients who had peptic ulcer, and among these there were 247 with a definite localization of the ulcer as follows: At the cardia, thirty-five to forty-two; lesser curvature, forty-three to fifty-three; pyloric, fifty-four to fifty-five; duodenum below fifty-five.

The immediate results have been satisfactory in all but four. Eight required operation soon after the period of duodenal feeding, four for pyloric obstruction, three for recurrent hemorrhages, and one for perigastric adhesion. Four patients had to be operated upon later, that is, from one to five years subsequent to the duodenal alimentation treatment, three of these for pyloric stenosis and one for recurrent hemorrhages. In fifteen there was a recurrence of ulcer symptoms from two to five years after the treatment. No deaths were encountered during the duodenal alimentation.

Concerning the results obtained, Einhorn says that not taking the late recurrences of ulcer symptoms after two years into consideration, the good results would be 95 per cent. Including later recurrences and necessary operations after two years period of benefit as failure, there would still be recoveries in 90 per cent. of those treated.

The treatment was applied in six cases of abundant recurrent gastric hemorrhages of the severest type, im-

mediately after this event, and perfect cures were effected.

The following brief outline of the plan of treatment is given:

The diagnosis of peptic ulcer having been made and the possibility of malignancy having been excluded with great probability, the patency of the pylorus is then ascertained (retention meal of rice or rice and raisins and the duodenal bucket string test). The pylorus not being stenosed (or not strictured to a great extent) the duodenal tube is then introduced and feeding by the tube begun as soon as the latter has reached the duodenum. The period of duodenal feeding is ordinarily two weeks, but can be extended for a longer time, whenever this appears appropriate. During the tube feeding period, the patient receives daily eight meals at two-hour intervals, consisting of milk (7 ounces), one egg, and from one to two tablespoonfuls of lactose; besides one pint to a quart of saline twice daily, likewise through the tube. As a medication the author usually gives subnitrate of bismuth gr. 30, in conjunction with calcined magnesia gr. 2 to 5, three times a day, in a wineglassful of water, by the mouth. A mouth-wash should be frequently applied, and the bowels should be made to move once daily either by medication or by enemas. For nervousness, tincture of valerian or a bromide may be employed and it is best given in the feeding through the tube. For pains, codeine or atropine may be administered in the same manner. The patient is ordinarily kept in bed during the first week of the tube feeding; the second week he is up gradually more and more each day. After the two weeks of tube feeding are completed, the tube is withdrawn and nourishment given by mouth, at first principally liquids, but very soon semisolids, and in about three days also light solid foods. At first the patient is fed every two hours, but as soon as he is on a liberal diet three ordinary meals and two small meals in between are instituted. The above-mentioned bismuth medication is continued for a month or two longer and then gradually discontinued.

**Perforated Gastric and Duodenal Ulcer.** An analysis of twenty-two instances of perforated gastric or duodenal ulcer that occurred in the Los Angeles County Hospital in 1916 to 1918, inclusive, is the basis of an article by Harlan Shoemaker.<sup>4</sup> Six of the patients in this group died. Twenty-two were divided among nine operators. Seven patients with ruptured ulcers of the stomach or duodenum in this group of twenty-two recorded cases had been previously treated medically for ulcer of the stomach or duodenum, in the Los Angeles County Hospital and discharged, as improved or cured, only to rupture. One perforation occurred within one month after leaving the hospital, while the longest quiescent period lasted two years.

An important point in a study of this kind has to do with how Nature will protect her subjects in such a catastrophe. Shoemaker says that any one of four possibilities will arise:

First, and most frequent, the ulcer, either gastric or duodenal, may rupture on the anterior, or free surface of the viscus, and the contents of the stomach spill over the transverse colon into the pelvis, or else drain along the hepatic flexure of the ascending colon, producing symptoms of appendicitis, and filling the pelvis with the discharge.

Second, the viscus may rupture laterally, and become adherent to the liver, the general abdominal cavity being entirely protected by adhesions.

Third, the viscus may rupture posteriorly and involve the pancreas (one case with hemorrhage and death is noted).

Fourth, a large abscess may form about a perforation and be walled off by the transverse colon (two cases, one death). All four classical perforations have an entirely individual set of symptoms.

Of the six patients who died in this group, one lived ninety days after the operation and died following the breaking down of the anastomosis due to an infection of a continuous linen thread used as the first stitch in the anastomosis. The second died from the breaking down of the abscess barrier, with contamination of the

(4) California State Jour. Med., January, 1920.



general peritoneal cavity and its attending inflammation. The third died from hemorrhage into the abdomen and stomach following perforation of the duodenum. The fourth died of hemorrhage after seventy-two hours, following a gastro-enterostomy. The fifth patient died due to an involvement of the pancreas, and sixth died as a result of general peritonitis.

It is pointed out that after rupture of an ulcer three phases present themselves:

First, the stage of contamination when no infection is present. At this time the patient will bear almost any exploratory laparotomy, or operation. Sixteen of the successful operations of this series were performed during this period. This stage generally lasts ten hours from the onset of the acute pain. A second phase occurs after contamination, after which the patient feels better.

A critical review of these histories adds very little to our knowledge of this period. It is generally passed over with the remark that "the patient feels better." The last stage, that of general peritonitis, begins with the recurrence of the pain and terminates fatally.

## SARCOMA OF THE STOMACH

**Primary Sarcoma of the Stomach.** In June, 1914, a case of round-celled sarcoma of the stomach which is here reviewed was reported, by A. R. Kimpton of Boston. Coincidentally Frazier published an article on gastric sarcoma in which he stated that of twelve cases of sarcoma of the stomach the longest period of survival after operation was fourteen years, while the remaining patients survived "two, two years; one, one year; one had recurrence in three years; and eight were reported as well from two to eleven months after operation."

The following case, also reported by Frazier,<sup>5</sup> is of particular interest in that the patient is alive and perfectly well, with no evidence of return of the sarcoma five years and ten months after an extensive resection of the stomach for a very rapidly growing sarcoma of the round-celled type.

The patient had discovered the tumor when she was

(5) Boston Med. and Surg. Jour., Dec. 25, 1919.

11 years old, but never spoke of it until after marriage, four years before Frazier saw her. It had troubled her more or less by occasionally being sore and painful. Within the last two years before she consulted Frazier, the tumor had increased in size gradually and had given more discomfort in every way. The digestive upset had been more frequent at times necessitating only liquid diet, but the patient never vomited.

With the exception of these attacks of "indigestion" she considered herself in perfect health and certainly appeared perfectly well.

At operation it was found that the tumor mass was local, so far as could be made out, although there were palpable somewhat enlarged lymph nodes. A partial resection of the stomach was done and posterior gastro-enterostomy was accomplished with some difficulty.

An illustration of the specimen is shown in Plate XX-A. Microscopic examination showed a solid growth of irregularly rounded cells separated into small lobules by connective tissue bundles, and with but little intercellular substances. In many of the cells the nuclei were eccentric. Here and there were mitotic figures and double nuclei were occasionally seen.

A diagnosis of round-cell sarcoma was made. The small tumors were examined as well as the larger. As the illustration shows, the tumors varied in size, some being pedunculated; were largely at the pyloric end of the stomach and did not cause any stenosis. The largest tumor was partly broken down. This is the usual condition found in the round-celled type, which is the most common type of gastric sarcoma.

A second bismuth *x*-ray was taken April 24, 1918, four years and four months after operation. It showed no indication of recurrence of the sarcoma (Plate XX-B).

Although primary sarcoma of the stomach is not the rarity it was once thought to be, it is still uncommon enough to warrant careful study of such cases. The proportion of sarcoma, among malignancies of the stomach, is usually stated now as being as low as 2 per cent., but might be higher were it not that sarcoma of the stomach is frequently mistaken for carcinoma and so is recorded erroneously.

Sarcoma of the stomach is divided into four groups, according to the origin. The true fibrosarcoma arises from connective tissue, the leiomyosarcoma from smooth muscle cells of the wall of the stomach, the lymphosarcoma from the lymphoid-nodules, and endothelioma from the endothelial cells of the blood-vessels. By some writers, endothelium is not classified as a form of epithelium, which accounts for the listing of the tumors of this tissue under sarcoma. It will be remembered that a sarcoma is a non-epithelial malignant tumor.

Since it is known that an abdominal tumor had existed in this patient for years it is possible that the tumor was originally a leiomyoma that had taken on malignant properties. Whether this case, then, is a rapidly growing form of leiomyosarcoma or a lymphosarcoma, a recurrence might have been expected earlier than five years after operation. It is to be hoped that nine years later, this patient will be alive to be reported as surpassing the record that Frazier has given of fourteen years' survival after operation for sarcoma of the stomach.

**Sarcoma of the Stomach.** An Algerian soldier was admitted to the wards of M. Loeper<sup>66</sup> on March 17, with the common, and very vague diagnosis of "enteritis." The man seemed to improve slightly for a time under the sun cure, but died with progressive cachexia on May 7.

The progress of the case was briefly as follows: The first manifestations were dyspeptic symptoms, loss of flesh, and vomiting, all of which increased progressively, then there appeared a mass in the epigastrium and ballooning of the abdomen. Palpation revealed a tumor, which might be taken for a cyst or an abscess; examination of the abdomen showed ascites, thought to be symptomatic of bacillary peritonitis. Loeper admits he did not attach enough importance to two signs—first, a biloculation of the stomach, which he wrongly attributed to adhesions and a stenosis; second, the presence of cells in the fluid returned after lavage, and which were thought to be lymphocytes. The history is that of all gastric sarcomas and may be taken as a model. Necropsy

(66) Prog. méd., Nov. 15, 1919.

showed the presence of a round-celled sarcoma of large size, on the anterior wall, penetrating into the cavity and projecting under the mucosa.

Virchow (1865) was apparently the first to call attention to these tumors, calling them "muscular sarcomas." Since then many more have been found, and as long ago as 1908, Burgaud collected over ninety. According to Lecène and Petit, the condition is more common in women, and between forty and sixty years of age.

It seems that simple inflammatory reactions have been confused with sarcoma, and some of these again may have been due to syphilis. Nevertheless the proportion of sarcomas to other tumors of the stomach is large. Perry and Shaw claim 10 per cent., but this is doubtful. In six years, Loeper examined histologically, fifty-three cancers of the stomach only one of which was a sarcoma. This latter is often a finding at necropsy or operation, for its clinical course is somewhat analogous to that of epithelial cancer.

Sarcoma of the stomach is always, and above all, more so than cancer, a *tumor*, and this is often the first manifestation. Of 100 case reports consulted by Loeper, tumor was present in ninety, and in thirty there was no preceding symptoms of consequence. In 66 per cent. of the cases the tumor was preceded by functional signs or by general ones—marked anemia in four, ordinary dyspeptic symptoms in sixteen.

On other occasions there were pains more or less localized, coming on in crises or continuous; in some there were vomiting and marked intolerance of the stomach. The variability and the polymorphism of the symptomatology depend on the extent of the mass and whether it develops toward the lumen of the stomach or into the abdomen. For this reason Burgaud suggests that two principal forms be recognized—the "endogastric," which in the majority of cases gives rise to digestive disturbances; and the "exogastric," which does so exceptionally.

When of some standing, gastric sarcoma is evidenced by four orders of symptoms: Pain, vomiting, tumor mass, changes in the general health. Pain is rather vague, sometimes not clearly localized, but may be

marked. Some pains depend on digestion, rarely early, as a rule, late or very late. These pains signify localization in the midgastric region or at the pylorus. Vomiting is found in about 10 per cent. Like pain it may be early, but is generally a late symptom.

The tumor is a hard swelling, generally epigastric, occasionally umbilical; frequently presplenic or subhepatic. It is large, may be round like a cyst or abscess, but more often is nodular. Sometimes the sense of resistance and induration is diffuse and board-like. The tumor is but slightly tender; in over half the cases it moves with respiration, and also from side to side by palpation. It is seldom lacking except when situated at the pylorus, but here we have another finding—gastric dilatation with presence of fluid and splashing in the fasting stomach. The residual fluid may amount to as much as 400 gms., and be blackish in color. Since most of the cases were met with prior to the discovery of the *x*-rays, not many radioscopic examinations have been made. Though Michels in his thesis (1916) quotes a few confirming the stenosis, the deformity of the organ and its dilatation. The last is not invariable, for sarcoma does not produce ectasia as in some intestinal sarcomas; in fact, the size may even be lessened by the invasion of the tumor-mass. At the present time, radioscopy should be done in every case, for it may enlighten us as to the location of the growth, on the obstacle it sets up to gastric functions, as well as the degree of distension and mobility.

There are two general symptoms, anemia and wasting. The latter is nearly constant, and may be considerable, as in Kehr's patient, where it amounted to twenty-six pounds in six months.

Sarcoma of the stomach, as a rule, develops toward the peritoneum, and a dozen case histories refer to ascites and ballooning of the abdomen, with sarcomatous nodules on the peritoneum. The spleen may be involved; likewise the liver and lungs in some instances. Enlargement of the subclavicular or inguinal nodes is decidedly exceptional, though subcutaneous nodules may be present, and their nature can be determined by biopsy.

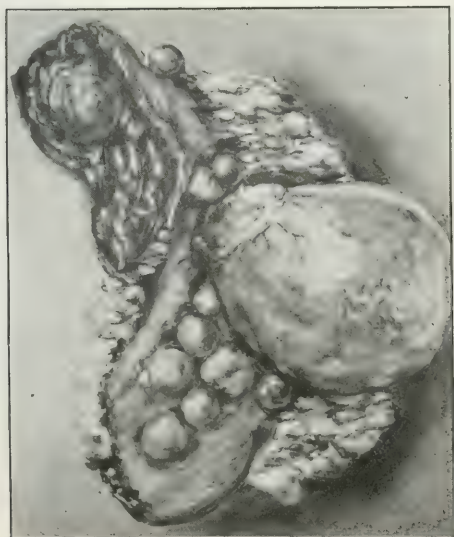
In structure these neoplasms may be spindle-celled or



PLATE XX.



B.



A.

Primary sarcoma of the stomach. Frazier, page 556.



round-celled. The former is less common, more benign, and more apt to grow toward the abdominal cavity. The other is much more common, is more malignant, and resembles the aspect of gastric cancer.

The round-celled variety is nodular, and may weigh from 1 to 1.5 kilos, but is always smaller than the spindle-celled type. It is made up of small round cells of variable size, most of them with mitosis. While the appearance resembles a lymphadenoma, there is no reticulum. Nevertheless some authors call it "lymphosarcoma." The leading feature is the presence of round cells, on which the diagnosis is to be based. These cells can also be found in the washings and should be carefully sought for.

While cytology affords great assistance in gastric cancer, and often enables early diagnosis to be made, it has seldom been used in sarcoma. Westphalen (1897) was fortunate enough to find tumor debris in the vomited matter, and histologic examination showed this to be sarcomatous; however, this occurrence seems to be unique. Loeper advises lavage, centrifugating the fluid, and coloration of the sediment. He admits, though, that in his own case, while this showed a considerable number of round cells, these were mistaken for lymphocytes. On re-examining the slides, he found the cells rather well preserved, of varying size, the nucleus very rich in chromatin, the protoplasm sometimes very abundant, a few multinucleated cells and a few mitoses. All these facts should have prevented error. Again, the cells were larger than lymphocytes, better preserved than the normal cells of the stomach, more resisting and more regular than those from an epithelioma.

As soon as the diagnosis is made, surgical intervention is called for at once, without delay. To tell the truth, the operation is satisfactory only in the exogastric tumors, *i. e.*, those which do not extend to the mucosa. Finding sarcoma cells in the wash-water shows this extension has taken place, and makes success doubtful, nevertheless the patient should be given the chance.

Out of twenty-two operations for the exogastric type and spindle-celled, fourteen were followed by survivals of from three months to as many years. In the true

gastric type, on the other hand, the operation is more delicate, and the results infinitely less good. Of nineteen operations, survival followed in but four. These discouraging results can be improved only by early diagnosis and equally early operation.

## SYPHILIS OF THE STOMACH

**Syphilis of the Stomach.** The apparent rarity of syphilis of the stomach, is due to the fact that this condition is not considered in some of the text-books of medicine and also to the fact that it is often overlooked or diagnosed as carcinoma, ulcer and various other common afflictions. Such mistakes are excusable, because the symptomatology and clinical findings in this disease have not yet been put on a sound diagnostic basis.

The following types have been described: Gastric ulcer of syphilitic origin, syphilitic tumor of the stomach, syphilitic stenosis of the pylorus, syphilitic cirrhosis of the stomach, chronic gastritis and perigastritis.

The symptoms most frequently encountered are pain, emaciation, tenderness, less frequently hematemesis and melena. In some instances, vomiting and pain after eating are the principal symptoms.

The record of a single patient in whom a diagnosis of syphilis of the stomach was made, is presented by M. F. Morris,<sup>6</sup> of Atlanta. The patient was a colored man, 33 years old, and he complained of inability to keep anything on his stomach. He had had symptoms related to the stomach for a period of two years. There was no nausea, but he would vomit almost everything that he took by mouth. Vomiting was projectile in type. Blood was not found in the vomitus, nor were the stools tarry. Rest in bed made the attacks much less frequent. Regurgitation of sour fluid was complained of. The appetite was good, but he usually vomited after eating a full meal. The presence of food in the stomach caused some pain, which was relieved by vomiting. He had lost a great deal of strength and about thirty-five pounds of weight since the onset of symptoms.

(6) New York Med. Jour., May 10, 1919.

The findings by physical examination were of little importance, except that the right pupil did not react to light or accommodation. Other reflexes were normal.

An analysis of the aspirated stomach content revealed the absence of free hydrochloric acid, combined acidity titrating 14. There was a small amount of lactic acid, giving a total acidity of 18, but no organisms were found. The Wassermann test was 4 plus positive. The Roentgenologist reported from the plates that there was probably a gumma of the stomach, a definite filling defect could be seen.

After studying several cases, and after reviewing much of the literature on this subject, Morris comes to the conclusion that syphilis of the stomach has no clear cut symptomatology and no certain clinical findings; that the diagnosis is best made by the process of exclusion; and that the *x*-rays are of great assistance in arriving at the correct diagnosis. He feels certain that many cases of syphilis of the stomach have been diagnosed as peptic ulcer or gastric carcinoma, also that every patient with ulcer of the stomach which does not yield to treatment by the usual dietetic measures, should have a course of antisyphilitic treatment before any surgery is done, and likewise that every case of suspected gastric carcinoma should be given a short intensive course of antiluetic treatment, in the hope that such a therapeutic procedure will establish the diagnosis of syphilis if it is present. The treatment of syphilis of the stomach should be the same as the treatment of syphilis in other organs. In those instances in which pyloric stenosis occurs, gastro-enterostomy is usually indicated in addition to the antiluetic treatment.

## BOTULISM

**Botulism from Canned Asparagus.** In January, 1919, four persons died at Boise, Idaho, as a result of eating asparagus that was taken from the jars and served cold in a salad. A portion of this salad, three jars of asparagus canned in the same pack as that used in the salad, and the cap of one of the two jars whose contents were incorporated in the salad, were procured.



and eventually turned over to Charles Thom, Ruth B. Edmondson and L. T. Giltner,<sup>7</sup> at Washington, D. C., for study.

The present article is based on their study of this material. They append notes dealing with the clinical condition of these patients, as secured from the local physician who cared for them.

The salad was taken at an evening meal. On the following morning, those who took the salad felt normal when they arose from bed. About noon a physician was called, and he found one patient complaining of a choking sensation in his throat, of a husky voice, a feeling of weakness, beginning in the feet and creeping upward. Within two hours afterward he became unable to talk. He had no pain, but breathing was labored and the pulse was rapid. While being transmitted to a hospital by ambulance soon after this, he died, and death was caused apparently by choking. There were seven negroes who were present at the meal at which the asparagus was served. Five of them ate the asparagus and four of these five died within thirty-six hours. The symptoms recited above were typical of the others. It was learned that the asparagus was home canned, cold-pack method, with single sterilization, and that at the time it was opened, one of the women remarked that it smelled spoiled. Microscopic examination of the salad, asparagus juice, washings from the extra cap in sterilized water revealed among other organisms *Bacillus botulinus*.

An extensive study, including animal experimentation was made with the organism, isolated from this food material. From the experimental data accumulated, the following examples were chosen as having a more or less direct bearing on the detection and elimination of danger from foodstuffs.

The thermal death point of the organism was tested. Cultures of this strain, which was named the Boise strain, in brain medium and glucose beef infusion showing an abundance of free spores were heated without pressure for varying periods of time at temperatures varying from 80° to 100° C. The organism survived

---

(7) Jour. Amer. Med. Ass'n, Sept. 20, 1919.

heating to 100° for one hour, but failed to grow in subcultures from tubes heated for two hours. In a series of tubes under pressure growths occurred in 50 per cent. of the tubes autoclaved at 10 pounds pressure for fifteen minutes, but no growth was observed after using 15 pounds pressure for fifteen minutes.

Other experiments were conducted which indicate that the toxin of this organism was attenuated somewhat by subjection to 68° C. for thirty minutes. The toxin is destroyed at some point between 70° and 73° C. by heating for ten minutes. When the temperature reaches 75° C. no appreciable period of heating is required to destroy it. It was learned also that the toxin is highly resistant to the action of light, since exposure to diffused light for two months and to direct sunlight for two, three, four and twenty-four hours respectively failed to diminish its virulence. Exposure to the direct rays of the sun for forty hours, however, destroyed the toxin.

Some of the cultures of this organism were placed in food materials and the food then placed in an ice box. This experiment showed that the organism can live and multiply in as low a temperature as 12° C. Therefore, food set away in the ice box is not free from danger, if *B. botulinus* happens to be present.

Successful canning, so far as the danger from such strains as the Boise organism is involved, depends not so much on the method of working as on the rejection of infected material at the start. Dirty, wilted and partly rotted food carries multitudes more organisms in the canning process than fresh, sound, clean fruits and vegetables. Dirty tables, dirty jars and lids, sewage polluted water and flies are sources of contamination which should be eliminated. The materials should be processed according to the best experience available. Finally, it must be frankly recognized that an occasional jar, or a series of jars may yet spoil because some factor escaped all these precautions. Such food should be destroyed, not salvaged, not fixed up into salads, nor pie stock for human food. The toxin present may be destroyed by heating until jar, lid and rubber, as well as contents have actually reached the boiling point. Typical spoiled cans are readily identified. Doubtful

cases, however, occur frequently. A consumer, unfamiliar with a particular product is frequently puzzled by its odor as it comes apparently sound from the can in good condition. Also, feeding suspected food to domestic animals without safeguards is clearly undesirable. Organisms have been shown to pass through the intestinal tract of animals, being recovered from the feces.

## INTESTINAL PARASITES

**Protozoal Infections of the Intestines.** That protozoal infections are not confined to the tropics is shown by the abundant evidence of reported cases studied by men in every part of the country. A contribution of this kind is made by R. Pollock and R. J. Pickard,<sup>8</sup> of San Diego, California, who observed forty-six cases in that vicinity during a period of one year.

By way of brief summary they state that endemic dysentery is caused by a distinct species of ameba (*Endamoeba histolytica*), an obligatory parasite, whose host, so far as is known definitely, is man. The disease can reach the intestine of men only by the ingestion of material containing *Endamoeba histolytica*, generally in the encysted stage. These amebas may originate from acute cases, or more commonly, from convalescent carriers, or even from individuals who have never had dysentery but are contact carriers. Such apparently healthy carriers on account of the cysts in their stools are more dangerous than the patient in the acute stage of the disease.

The flagellates (cercomonas, trichomonas, tetramitus) have not until recently been generally regarded as pathogenic. For this reason they have not been so thoroughly studied, nor have means of combat been so much searched for. In Panama, the chief interest they called forth was the frequency with which they were associated with amebas, demanding more careful search for the latter. Trichomonas, the flagellate most commonly found, does not form cysts so far as known, the so-called cysts being *Blastocystis hominis*.

A few facts related to treatment of these conditions

---

(8) Amer. Jour. Med. Sci., April, 1919.

stand forth as apparently proved. Ipecac in some form seems to have a distinctly beneficial effect upon the symptoms and plays a part in practically all methods of treatment directed against the amebas, although upon the flagellates it seems to exert only temporary influence.

The only method used by the authors that proved at all satisfactory in the treatment of flaggellate trichomonas intestinalis was the giving of large doses of calo-

Case No.	Reported in detail.	Sex.	Age.	Place of original infection.	Clinical symptoms.	Protozoa.
1	r	M.	26	South America	Dysentery	Ameba histolytica
2	r	M.	23	Mexico	Dysentery	Ameba histolytica
3	r	M.	43	South America	Hyperchlorhydria	Ameba histolytica; oxyuris; bothriocephalus, round-worm
4	..	F.	35	United States	Dysentery	Ameba histolytica; trichomonas
5	..	M.	65	.....	Achylic diarrhea	Trichomonas
6	r	M.	47	Philippines	Nervous exhaustion; hypochlorhydria	Ameba histolytica; trichomonas
7	r	F.	43	Minnesota	Diarrhea; hyperchlorhydria	Trichomonas
8	r	F.	47	Mexico	Fever; chills	Trichomonas
9	..	F.	46	.....	.....	Trichomonas
10	r	M.	68	Wisconsin	Anemia (emicious?)	Ameba histolytica; trichocephalus
11	r	M.	38	Mid-West	Intermittent diarrhea	Ameba histolytica; trichomonas
12	..	M.	50	South Africa	Intestinal indigestion; constipation	Ameba histolytica
13	..	M.	59	Mexico	Dysentery	Ameba histolytica; uncinaria; strongyloids
14	..	M.	58	New Jersey	Dysentery	Ameba histolytica
15	..	M.	40	North Carolina	Dysentery	Ameba histolytica
16	..	F.	40	Nebraska	Constipation	Ameba histolytica and monads
17	r	M.	37	Cuba	Attacks of somnolence	Ameba histolytica; trichomonas
18	..	F.	65	Japan	Diarrhea; achylia	Ameba histolytica
19	r	M.	43	Northern U. S.	Diarrhea	Trichomonas

mel followed by saline purgation, once every four or five days, coupled with daily colonic irrigation with mercuric chloride (from 1 in 10,000 to 1 in 20,000).

In a group of forty-six cases coming under the notice of the authors during the past year, with symptoms seeming to demand a careful search for intestinal parasites, nineteen or 41.3 per cent. showed protozoal parasites, many times accompanied by other intruders. So frequently have the trichomonas presented association with troublesome and even grave symptoms that this

organism is considered by the authors the direct cause of certain forms of acute, chronic and recurring enteritis, with abdominal pain, diarrhea, loss of weight, elevation of temperature, and at times anemia.

While this group of patients is considered too small as a basis for statistical analysis, yet the suggested prevalence of these diseases in the communities noted is worthy of attention. The essential facts connected with these nineteen patients are tabulated in the accompanying table.

In conclusion the authors emphasize the fact that San Diego County undoubtedly contains many cases of protozoal infection, more or less active, as well as many convalescent carriers. Some of these cases from northern latitudes probably become more active by reason of the climatic change, the effect of a marked change of climate and latitude upon the virulence of protozoa having long been known.

**The Broad Tapeworm, *Dibothriocephalus Latus*.** Cases of infestation of man by the broad or fish tapeworm, *Dibothriocephalus latus*, have been regarded as rare in the United States. Nevertheless one author has stated that over thirty cases have been recognized here, chiefly among foreigners, at least four cases have been reported since that time, and the present author, William A. Riley,<sup>9</sup> has knowledge of seven cases from Minnesota which have not been recorded.

In 1906 Dr. W. S. Nickerson reported three cases that had occurred in the practice of Dr. O. W. Parker, of Ely, Minn. The patients in two of these cases were Finns, but the most significant fact was that the third was a child of Finnish parentage, who was born in Minnesota and had never been outside of the United States.

So far as the author has been able to determine, Dr. Parker's case is the only recorded one of *Dibothriocephalus* infestation of man in this country which is not clearly explicable on the theory that the parasite was an importation.

The general view of medical men is that there is very little evidence at present to justify the assumption that many foci of infection exist in this country. For these

(9) Jour. Amer. Med. Ass'n, Oct. 18, 1919.



reasons it seems desirable to the author to place on record two additional cases which came to his attention in the course of studies on the subject. In both of these available data are very meagre, but the essential facts bearing on the question are clear. In neither case was there any doubt that the condition originated in Minnesota. The first patient was a Minneapolis boy, aged 8 years, who had been suffering from gastric trouble. On treatment a specimen of *Dibothriocephalus*, 7 meters long, including the head, was dispelled.

The second patient was a young Chippewa Indian child on the White Earth Indian Reservation, Mahnomen County, Minn. This child had never been away from the reservation, but was infested by a *Dibothriocephalus*. On treatment, more than 3 meters of proglottides were removed.

Complaint of fish containing tapeworms have been made to the author in this section of Minnesota, but on investigation, it was found that the supposed tapeworms were larval trematodes encysted in the flesh of the fish. In the case of several small-mouthed black bass there were in the viscera numerous proteocephalid tapeworm larvae, classified as *Proteocephalus ambloplitis*.

It is said, however, that the possibility that there may occur in this region bothriocephalid larvae other than those of *D. lacus*, but equally capable of developing in the human host, is strong. Their development in the dog as observed by Hall and Wigdor in Detroit is suggestive, but the question as to the relation to man can be settled only by direct experimentation, as opportunity offers.

**Lambliæ-Enteritis.** In the course of about a year, Cade and Hollande<sup>10</sup> had under observation some ten cases of enteritis due to *Lambliæ*—or *Giardia*—*intestinalis*. This parasite has four pairs of flagella; in the human intestine it adheres to the epithelial cells by its peristome something in the manner of a cupping-glass.

In the feces it is rarely found alive, moving more or less quickly by its flagella, sometimes it is motionless; in addition to the free stages, encysted ones are seen very often. These last are oval and not circular as are

(10) Archiv. d. mal. de l'app. digest., July, 1919.

amebas, they are transparent and observed under the microscope with some difficulty. In size they are from 10 to 13 microns long by 8 or 9 microns wide. In "carriers" the cysts are often seen in a state of degeneration; also after use of certain drugs.

Since the parasites die rapidly in the feces after expulsion, even at room temperature, it is evident infection cannot take place by the free adult forms. On the other hand, the cysts preserve their normal aspect if kept in a moist place, though if dry they also degenerate quickly. It is possible the transmission takes place between individuals either by the cysts in water or by direct contagion. In addition, judging by the observation of Wenyon and O'Connor (1917), flies may be responsible, the cysts may pass through the digestive tube of these insects unchanged. Lastly, another species, *G. muris*, is found in mouse feces, it may be this is the same species, and food may be thus contaminated (Fig. 20).

In one case, Cade and Hollande found association with eggs of *Trichocephalus*, and in another with numerous spirilla. The presence of *Endamoeba dysenteriae* is especially to be remembered and sought for. Often one is dealing with old dysenteries. The ameba or its cystic form appear only at rare intervals, and are found, *c. g.*, after a diarrheal recrudescence, either spontaneously or provoked by drugs. On account of this association with other animal or vegetal parasites, some authors believe it is merely an associate, and only aggravates pre-existing lesions, either directly or by inoculating microbes in the bowel wall. Cade and Hollande believe this may be possible in some instances, but does not preclude the *Giardia* being directly responsible on occasion. However, its mere presence does not give rise to enteritis; and there may be healthy carriers.

Before the world war the cases of this enteritis were few in number. Since then a large number have been encountered, especially by English observers: Woodcock and Penfold (1916) of ninety-eight examples of protozoal infections of the intestines, found twenty-two were due to *Giardia*. Wenyon (1916) examined the stools in 556 cases from the East, and found 295 with protozoal infection, either simple or mixed, and eighty-

nine of these in turn were due to *Giardia*. In soldiers coming from the Dardanelles, Fantham and Porter (1916) discovered 187 instances of pure lambliosis among 1305 patients. Jepps (1916) examining the stools of 426 soldiers in the Mediterranean army, on sick-leave for intestinal affections, found *Giardia* eighty-one times; in pure state, fifty-three times. At the Liverpool Institute for Tropical Medicine, this parasite was found in 18.6 per cent. of 910 examinations.

However, it seems equally prevalent in temperate countries, and none the less virulent. In fact some cases

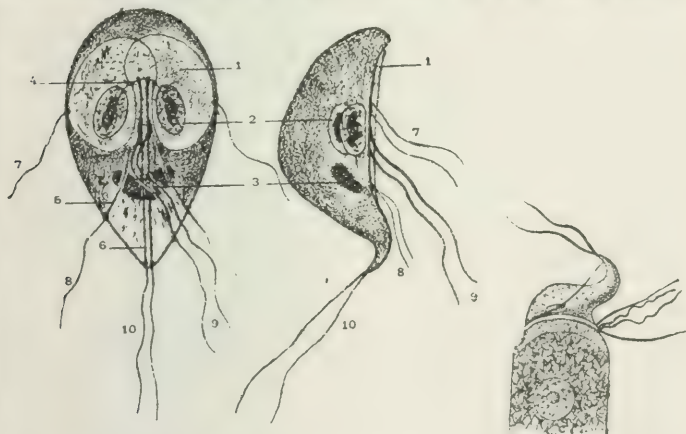


Fig. 20. *Giardia intestinalis* — face and profile (Cade-Hollande, after Wenyon-Bensen).

1, peristome; 2, principal nucleus; 3, body of enigmatic nature; 4, arched rhizoplast with four blepharoplasts; 5, oblique ribs; 6, ventral ribs; 7, 8, 9, 10, flagella.

At right, *Giardia* (*Lambia*) adhering to an epithelial cell of the intestine (Cade-Hollande, after Grassi-Schewiakoff).

from Flanders were more virulent than those from the Orient. Of the ten patients seen by Cade and Hollande only two were from the colonies. No doubt some of the apparent increase is due to the fact that systematic examination of the stools was undertaken, but the infection was facilitated by the army life, poor food, overcrowding, etc.

From the standpoint of symptoms, the chief characteristic is diarrhea. The onset is not very violent, and

may make little impression on the patient. The stools number from four to six in the twenty-four hours, sometimes fewer. But there may be exacerbations, when the number rises to ten, fifteen or even twenty. Functional disturbances are not very marked, though colics precede the bowel movements rather often; but as a rule, these are either absent, or seen especially with the exacerbations. The temperature may remain normal for a long time at least; though evening rises of slight intensity are not rare ( $100.3^{\circ}$ ,  $100.8^{\circ}$  F.). In one patient the elevation was higher ( $103.2^{\circ}$ ,  $104^{\circ}$  F.), and after persisting for a few days, fell by lysis.

Judging by their experience, Cade and Hollande are of the opinion that the development is of long duration, interrupted by exacerbations these in turn being followed by periods of calm. In one patient there was a history of duration for a decade. It seems too soon to form any conclusion as to the prognosis. In some individuals the affection is benign, almost latent, not interfering with activity except when there is a recrudescence. Others on the contrary, are more disturbed and obliged to seek medical advice.

Evidently the only way of reaching a diagnosis is by examination of the stools under the microscope. During the exacerbations discovery of the adult parasite or its cysts will not be very difficult. Where cysts alone are found, and not very common, this search will be facilitated by a previous dose of some slight purgative (15 gms. of sulphate of soda). This microscopic examination will enable elimination of other agents, especially *Eudamcha*, *spirilla*, *Trichocephalus*, *Ascaris*, *Ankylostoma*, *Balantidium coli*, as well as other flagellates than the *Giardia*, and especially *Trichomonas*. Nevertheless, the mere finding of the *Giardia* does not prove it is the sole cause. The clinician must, by a careful study, eliminate other diarrheal affections, in which its presence may be a mere coincidence and not of etiologic importance.

The treatment is far from settled, the rebellious nature of the affection explains the multiplicity of drugs used. While the diet must not be neglected, it alone is insufficient; as a general thing it has been the same treatment

as for the common intestinal dyspepsias. The quantity of cellulose in the stools in similar cases, shows that vegetable food leaving much of this residue must be prohibited.

Prepared chalk in large doses gives a simple amelioration of the intestinal troubles. Ipecac is totally insufficient. Injections of emetine, even in large enough doses and repeated in series, give very uncertain results, and invariably not sufficient. The double iodide of emetine and bismuth also failed.

Wenyon gave drastic cathartics but could not destroy the *Giardia* completely. He had the same failure with calomel, as with vermifuges generally; though Deglos noticed great improvement on three occasions by the use of thymol. One of Cade and Hollande's patients also improved under thymol, but here there was association with *Trichoccephalus*, and the latter alone disappeared. While salicylate of bismuth in large doses (15 gms. daily), is often efficacious, it is inconstant, and sometimes followed by untoward effects. Betanaphthol also in large doses, seems capable of destroying the parasite, but is inconstant: Cade and Hollande saw no effect in two cases. Woodcock and Penfold advise a combination of this with the bismuth salicylate.

Speaking generally the former authors point out that to judge the results from treatment, repeated examinations of the stools must be made. The adult *Giardias* and the cysts vary much in number, irrespective of the treatment. Hence the temporary disappearance is no criterion of a cure. Nevertheless, should such intermission be prolonged, the effect can rightfully be attributed to the therapeutics.

The clinical phenomena also need delicate interpretation: Spontaneous—though very transient—improvement is frequently noted. However, the disappearance or very marked lessening of the diarrhea, particularly if of long standing, is an interesting and favorable result of the action of a given medicine. On the other hand, the persistence of the intestinal troubles after the parasite and its cysts disappear from the feces, does not signify the disappearance is not final, the lesions of the bowel may be too deep and too old not to keep up for



some time, at least, after the causal agent has been destroyed. The prime reason for the stubborn nature of lambliosis is the penetration of the parasite and its cysts deep into the intestinal tunics. The cysts escape the destructive agent, and appear once more when treatment is suspended.

As in amebiasis, medicines introduced by the blood current appear to act more energetically on the parasites enclosed in the intestinal tunics, and it seems rational in all cases to repeat the therapeutic intervention at different times. Finally, the fact that the parasite multiplies in the small intestine explains why medicated enemmas useful in amebiasis and in *Trichomonas* are of no avail.

**Hookworm Infection.** This paper by Samuel T. Darling<sup>1</sup> is prepared from data obtained in Malaya and Java in 1915 and in 1916 by the Malaya Board working under the auspices of the Colonial Office and the Rockefeller Foundation and by the support of the latter.

A considerable portion of the work has to do with the relation between hookworm and the anemia produced by it.

From figures obtained in this investigation it would appear that in hookworm infection, when measurable amounts of anemia are produced, one degree of anemia, or the loss of 1 per cent. of hemoglobin, is caused by about 10 worms in women, 7.6 in boys (9 years of age), and 11.7 worms in men.

These factors may be used in a community in estimating the amount of anemia or blood loss caused by hookworm in the presence of malaria or other cause, as hard labor and under-feeding.

In the district where this work was carried out many coolies arrived, and were sent out to various estates as laborers. Definite advantage was obtained by giving a preliminary hookworm treatment to these coolies before sending them out to the estates. The advantage shown by figures tabulated in the report. When they go to an estate and contract malaria, their blood loss as shown in recorded anemia is not so great as it would have been

---

(1) Indian Med. Gaz., December, 1919.

had they not received the hookworm treatment before being sent out.

Emphasis is placed on the point that malaria and hookworm infection are often associated and coöperate in causing the anemia of peoples in tropical and sub-tropical lands.

The over-powering nature of malaria in causing anemia is well shown in figures that are presented, in which the amount of anemia on an estate is directly related to the incidence of malaria as disclosed by the blood and spleen test and irrespective of the associated hookworm infection. That is, in addition to the anemia already caused by hookworm, an additional and increasingly heavy burden is placed on the blood-forming organs as the degree of malaria increases.

The gross average change in hemoglobin in coolies after residence on the estate, irrespective of treatment or new infection of hookworm, is shown in relation to the incidence of malaria in the same estate.

The following comparison of four commonly used vermicides in moderate doses is presented:

#### EFFICIENCY OF VARIOUS VERMICIDES.

Treatment	Valid cases	Worms removed by first or trial treatment, per cent.
Betanaphthol, 20 grains in capsules, 2 doses with 2 hours' interval.....	10	26.7
Eucalyptus, 30 minims, chloroform, 45 minims, and castor oil to 12 drams divided into two doses of 6 drams each, and given with 2 hours' interval.....	10	46.9
Thymol, 30 grains, in emulsion 2 doses with 2 hours' interval .....	10	88.6
Oil of chenopodium, 1 c. c. in capsules two doses with 2 hours' interval.....	8	96.15

In the comparison of drugs chosen and given in medium doses, oil of chenopodium is the most efficient.

The efficiency of oil of chenopodium in various dosages was next tested. For this purpose seventeen patients were treated, and the oil was given in 1 c.c. doses in capsules, three doses at hourly intervals, or 3 c.c. alto-

gether. It was found that 98.9 per cent. of worms were removed by trial treatment in these cases. This size of the dose and the interval between doses each were varied and no other combination gave as good results as the above.

The method of treating hookworm infection by giving two or three treatments of chenopodium, 1 c.c., is therefore highly recommended. It would be possible to treat the entire agricultural population of a given district. Southern India is mentioned here, with this method, without the necessity of examining the stools microscopically for ova, for nearly 100 per cent. of the people over 12 years of age in the district mentioned, were infected.

The effect of varying the diet and omitting the first purgative dose on the result obtained with oil of chenopodium is indicated in the following table:

Diet used	With purge		Without purge	
	Valid cases number	Worms removed per cent.	Valid cases number	Worms removed per cent.
Diet 1: Full diet all through the treatment .....	5	44.5	5	57.1
Diet 2: Full diet all the day previous to treatment, but milk on morning of treatment.....	4	88.7	4	87.5
Diet 3: Rice gruel (kunji) on the afternoon previous to treatment, but milk on the morning of treatment .....	4	92.	5	95.7
Diet 4: Only milk during the day previous to treatment and only milk on the morning of treatment .....	12	78.7	14	56.3

It is seen that there is a steady increase in the percentage of worms removed with the increase in the amount of deprivation up to Diet 3, or the diet used in the routine preparation of cases. When the starvation is increased beyond this, a remarkable drop in the percentage of worms removed was noted.

It is concluded from this work: First, the initial

purge may under certain circumstances be omitted without altering very much the efficiency of chenopodium treatment. This would lessen the work of the dispenser and permit a large number of people to be visited. Second, it is extremely important in order to exert the maximum toxic effect on the worms that food be withheld during the morning of administration, and that the evening meal before treatment be light and digestible, leaving little residue.

The stomach and small intestines should be as free as possible from food or chyme whenever treatment is begun, for the latter seems to lock up and absorb some of the chenopodium, leaving a smaller portion to come in contact with the worms.

**The Treatment of Hookworm.** Since it is known precisely that the human habitat of the hookworm is the first portion of the jejunum, with extension along the intestine in both directions in the severer infections, it follows that the parasites can be removed with the greatest despatch by a method which would permit of the direct introduction into this region of a maximum concentrated dose of a drug chosen for this purpose. A scheme devised to accomplish this and which has been used in the United States Army, is reported here by John L. Kantor.<sup>2</sup> The procedure is as follows:

The evening before treatment the patient is given a light supper, usually rice and milk. There is no preliminary catharsis. The next morning at about 7:30 the duodenal tube is swallowed on a fasting stomach and the patient is kept on his right side until the bucket has passed the pylorus. The exact time at which the intestine is entered can be determined by the accompanying differential tests:

Differential Tests: Bucket in Stomach.—Aspiration through the tube withdraws a clear fluid, seldom bile-tinged, generally positive to Congo paper.

If a definite amount (say 15 c.c.) of water is injected, and the injection is followed by a syringe of air to clear the tube, the greater part (more than two-thirds of the water) can be withdrawn on the next aspiration.

(2) Jour. Amer. Med. Ass'n, Oct. 18, 1919.

Injection of air is not followed at once by borborygmi.

Bucket in Duodenum.—Aspiration withdraws golden yellow, viscid bile, negative to Congo paper.

The water injected flows on into the intestine and but a small amount (less than one-third if any) can be recovered by aspiration.

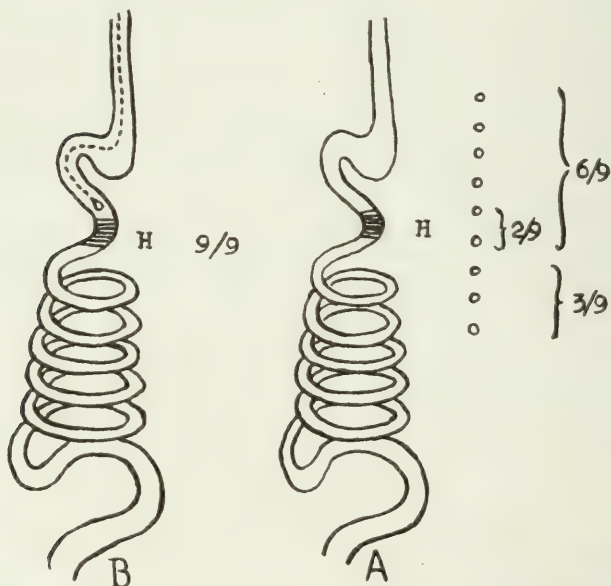


Fig. 21. The shaded portion, *H, H*, represent the region occupied by the hookworm. *A* represents the digestive tract in a hypothetical "mouth" treatment with the drug given in three capsules, one every hour for three hours. The nine capsules are arbitrarily represented as dissolving opposite the levels indicated by their position to the right of the "tract." In case, for example, two of the capsules dissolve exactly opposite the infected area, four capsules above this point, and three below, the patient would receive the maximum benefit from two-ninths of his dose, some benefit from six-ninths of his dose, and none at all from the remaining three-ninths. In the case of the "tube" treatment, *B*, the patient is represented as receiving the entire dose, nine-ninths, with corresponding increased efficiency.

Injection of air is followed at once (in some cases) by borborygmi.

As soon as Congo-negative bile is obtained, and water can not be recovered, as described above, the patient is ready to receive the drug. This is injected directly with



a syringe (preferably of glass and of about 30 c.c. capacity), and is followed by a barrel or two of air to insure the expulsion of the entire dose from the tube.

The drug used in the work reported here was oil of chenopodium, and it was commonly given in doses of 3 c.c. Following the injection a period of six minutes is allowed for the diffusion of the oil throughout the worm-bearing area. At the expiration of this interval, from 2 to 3 ounces of a warmed saturated solution of magnesium sulphate are given transduodenally. The object of this flush which is regarded as a very essential part of the treatment is to remove the drug quickly from the very highly absorptive small intestine, in order that undue toxic effects may be avoided. That this is actually accomplished is indicated by the observation that the majority of patients have a copious watery stool containing oil, and sometimes worms, within half an hour following this procedure. The regularity with which this sequence follows is one of the most striking features of the treatment.

It is stated incidentally that this flush method of control opens the way to the safe use of drugs in doses ordinarily considered dangerous. At different times the author has administered as much as 4 c.c. of oil of chenopodium, 12 grains of santonin, and 12 gm. of oleoresin aspidii without undue disturbances.

After the salts are given, the tube is removed and the treatment is complete. In most instances from three to five stools follow the first. If a sufficient number do not result, further catharsis may be administered by mouth. The patient is generally sick during the day of treatment, but at supper time is ready for a light meal and feels as well as ever the next morning.

While systemic symptoms have been produced by this form of treatment, no serious results have been observed at any time.

**Treatment of Hookworm in Soldiers.** A study of hookworm infection among soldiers and of treatment of this infection with oil of chenopodium, is recorded by R. H. Knowlton.<sup>3</sup>

The work was done at a military hospital and accord-

(3) Jour. Amer. Med. Ass'n, March 8, 1919.

ing to the routine treatment used there a light supper was ordered the night before, and a full dose of magnesium sulphate given about eight o'clock in the evening. No breakfast was taken in the morning, and 1.8 c.c. of oil of chenopodium was given in six gelatine capsules, supplied by a pharmaceutical house—two every hour for three doses. Two hours after the last capsule another full dose of magnesium sulphate was given.

A similar group of patients were treated in the same way with the same oil expressed from the proprietary capsules. The oil was collected in a graduate and measured in a pipet, and exactly 0.3 c.c. put into hard gelatin capsules, which were very soluble in water. In every case, whatever the laboratory findings have been, each patient received at the end of four days a second treatment with freshly expressed oil and this was repeated at similar intervals until it was evident that all worms had been removed.

Based upon the results obtained by these two methods, the efficiency of the capsules was rated. That of the soft capsules was found to be 68.5 per cent. and that of the fresh oil 94.5 per cent. The question arose immediately as to what this marked difference was due, whether to a lack of dosage in the soft capsule or to its lack of solubility.

Darling, Barber and Hacker are quoted as having determined that the insolubility is the main factor, as even 0.75 c.c. of fresh oil was superior to the soft gelatine supposed to contain  $\frac{1}{2}$  c.c.

From this work the authors learned that while in a considerable proportion of soldiers this infection was light, all grades were encountered and a few were classed as severe. The negro appeared to be less severely infected than the white race. The soft gelatine capsules stated to contain 5 minims were distinctly less efficient than a similar dose placed in soluble capsules.

## INTESTINAL OBSTRUCTION

**Intestinal Obstruction.** A study of the factors involved in the production and absorption of toxic materials from the intestines has been made by L. R. Drag-

stedt, A. Dragstedt, J. T. McClintock, and C. S. Chase,<sup>4</sup> in the Laboratories of Physiology and Pharmacology of the State University of Iowa.

The experiments were performed on dogs under complete ether anesthesia and with strict aseptic precaution.

In discussing the results obtained in this work, the authors state:

It has been definitely determined that death resulting from acute obstruction of the intestine is due to a toxemia and that the responsible toxic substances are formed in the obstructed intestine. These toxic substances can be found even if all food materials, end-products of digestion, and the secretions of the stomach, liver, and pancreas have been carefully excluded.

The secretion of the intestinal mucosa is not toxic either when absorbed from the abdominal cavity or injected intravenously. The mucosa of the alimentary tract (stomach, duodenum, jejunum, ileum, or colon) does not elaborate an internal secretion which is necessary to life, or which could be disturbed by the condition of acute obstruction so as to account for the symptom-complex of that condition.

The presence of bacteria in the lumen of the intestine is necessary for the production of the characteristic toxic substances and in their absence these substances do not form. They are produced by the action of the intestinal bacteria on proteins or their split products. In the absence of food, gastric juice, bile, or pancreatic juice, these bacteria can produce the characteristic toxic substances from the intestinal juice or from the proteins of desquamated mucosa cells. The important poisons will not provoke the appearance of immune bodies when injected in experimental animals and it could not be demonstrated that an animal can become immune to the toxemia of acute obstruction.

Toxic amines are produced by the action of various intestinal bacteria on amino-acids and the evidence more and more points to these substances as the important agents in the toxemia of acute intestinal obstruction.

The toxic substances arising in the lumen of the obstructed intestine are not readily absorbed through a

(4) Jour. Exper. Med., August, 1919.

normal mucosa. Nor are they absorbed to any great extent through the mucosa of a closed intestinal loop until this mucosa has been injured by the distention of the loop and the consequent interference with the blood supply. If this distention is prevented by any means, absorption of poisons in quantities greater than can be cared for by the liver tissues does not occur. Thus it appears, that the injury to the mucosa cells, either as a result of the sudden distention brought about by conditions of obstruction or by any other factors which interfere with the blood supply to the mucosa (strangulation, etc.) is an important factor in the absorption of toxic substances from the intestine. There can be no doubt that necrosis of the mucosa greatly facilitates the absorption of intestinal poisons; but it is incorrect to say that intestinal poisons, *i. e.*, those found in obstruction, can not be absorbed through a normal mucosa. The protective action of the intestinal mucosa exercised through its properties of selective absorption is not absolute, but that it is of great significance is shown by the fact that an animal can take care of the amount of poisons absorbed through the normal mucosa of a short closed intestinal loop which has been treated with astringents, but that as soon as this mucosa becomes necrotic an overwhelming amount of toxic material gains entrance to the blood-stream, and toxemia and death occur. The absorption in these cases can not be different from absorption from the peritoneal cavity.

## THE CECUM

**Gumma of Cecum.** This condition was discovered by D. Giordano<sup>5</sup> the Italian surgeon during an operation for appendicitis: A man, of 54, some three days previous without appreciable cause, was suddenly seized with acute pain in the ileocecal region. The passages were loose, but there was no vomiting. He took some castor oil, but this gave no relief, so he consulted a physician, who sent him to hospital. The man asserted he had never had any gastric disorder, though a heavy eater

(5) Archiv. d. mal. de l'app. digest., July, 1919.

and drinker. He also denied venereal disease, though he had been married six years and had no children. In spite of his assertion, he was thin, and seemed overworked, the tongue was coated and the abdomen distended. The second heart sound was accentuated; there were traces of albumin in the urine.

The ileocecal region was slightly prominent and tympanitic. The pain was not increased by pressure, on the contrary, it was more marked if the hand compressing the area was withdrawn suddenly. Deep palpation revealed a resisting nodule, almost fixed, which was interpreted as an infiltrated appendix.

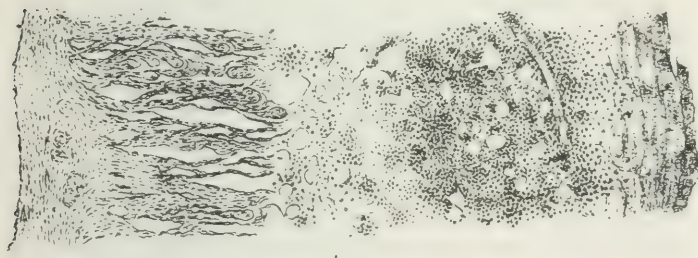


Fig. 22. Histologic structure of gumma of cecum (Giordano).

The mucosa is necrosed, and the submucosa the seat of a diffuse infiltration of small cells, which show a tendency to collect here and there into groups. The submucous layer of connective tissue itself is considerably thickened. There is diffuse hyperemia and formation of new connective tissue about the vessels, the wall of these latter is thickened also. All these characters prove the specific sclero-gummatous nature of the lesion.

Operation was accordingly undertaken for supposed chronic appendicitis with an acute exacerbation. When exposed, the appendix was the size of the little finger, twisted and adherent to the external surface of cecum, but on the cecum itself, 3 cm. above the origin of the appendix, and on the anterior surface was a circular depression nearly 3 cm. wide; palpation here showed that there was thickening of the wall of the cecum, with a tumor growing into the lumen. The appendix after being freed was removed *en bloc* with the part of the cecum containing the tumor.

The tumor was deep red before excision, but soon be-



came pale. The mucosa at the edges was granular but rapidly became of normal aspect. On section it was hard, grayish-white, and apparently mostly developed in the inner tunics of the bowel. The gross appearances were so like those of a gumma, that Giordano ordered the man given an injection of 10 cg. of calomel. Recovery was uneventful.

Histologic examination of the appendix showed chronic inflammation though it does not seem correct to term it "syphilitic appendicitis."

## COLITIS

**Spastic Colitis.** In this paper, A. W. White,<sup>6</sup> first calls attention to the existence of a condition of the colon, non-surgical, but having definite anatomic changes, and of different types, a common classification being ulcerative, mucous, spastic and membranous.

The ulcerative type is rare. The other types are merely stages of the same condition. That is, in every case of spastic colitis, the evidences, varying in degree, usually attributed to mucous colitis, are present, and there may occur such shedding of epithelium along with the mucous to amount to the so-called membrane.

Physicians are prone to consider these patients as suffering from auto-intoxication, bowel stasis, etc., and the accompanying symptoms as those of toxemia, and to force elimination by heavy cathartics, which may relieve the situation temporarily, only to have it return worse than before. White considers that the greater part of the symptom-complex is reflex and is due much more to disturbance of the nervous system than to any other cause. The majority of these patients complain of a feeling of discomfort, with pains varying in intensity and frequency a few hours after eating or just before defecation. There is a feeling of tension or bloating in the abdomen which may be relieved by the passing of gas. Occasionally, the flatulence may become so severe as in itself to be responsible for other symptoms, as the shortness of breath, angina, palpitation, etc.; more often, however, it is merely sufficient to produce pressure

(6) Jour. Oklahoma State Med. Ass'n, March, 1919.

against the stomach, so that the patient interprets it as gas in the stomach and an effort is made to belch, which gives momentary relief. These patients mostly report belching of gas, but as they are observed one soon discovers that no gas is brought up, other than the air that has been swallowed in the effort of belching. Symptoms common to most of these patients are colicky pains in the abdomen, general sluggishness, variable appetite, sense of weight over the lower abdomen, tenderness of the plexuses of the abdomen and along the course of the colon, all or in part depending on the part of the colon involved. The stools are either mushy or formed, but of small caliber and alternating, with an unsatisfied feeling after defecation as though the action were incomplete. Constipation may or may not be present.

Among the author's patients suffering with this complaint, constipation was present in more than 60 per cent. of them. These patients consult the physician either because of the disturbance of the stomach, or lunago, or nervousness in a greater or less degree, hysterical outbreaks, neurasthenia, melancholia: they are frequently self-centered and easily worried: they experience difficulty in getting to sleep, and have inability to concentrate.

The diagnosis, as a rule, is not difficult if one is careful to note the character of the stool. The rule is a tendency to constipation with small formed stools, varying with stools that are very soft or mushy, practically never a normal stool. This, together with the evidence referred to above, usually makes a clear cut case.

The final positive diagnosis, however, should not be made without first excluding all other suggestive possibilities. The stomach being so susceptible to reflex effects is almost always disturbed functionally, either a hyperchlorhydria or a hypochlorhydria is present and may produce symptoms sufficient to focus the patient's attention on it.

The treatment of these patients consists, in those cases which are primarily bowel affairs, in first bringing about a complete relaxation of the bowel, and this is best accomplished by rest in bed, if the condition is at all marked. The diet ranks almost with rest in importance.

Foods that are stimulating or irritating to the bowel, such as meat, yeast bread, fruit, raw vegetables, salads, etc., are not to be permitted. Only foods having a non-irritating residue, or no residue, and which are not stimulating to secretions are to be employed, as cereals, hot boiled milk, soft eggs, puree soups, and soft vegetables; frequent feedings in small quantities being prone to allay peristalsis and encourage mass movement are much preferred.

In case of marked colonic spasm with constipation, heat at 110° F. applied at hourly intervals, gives good results. If the pain due to spasm is persistent, a warm enema given slowly and retained and repeated as often as necessary gives the quickest relief. For constipation a retention enema of a vegetable oil at night, and if necessary followed by a low water enema in the morning to secure a bowel movement is recommended. It is not probable that the oil has any positive healing effect, its only value being as a substitute for a laxative cathartic, which must not be given on account of the stimulating effect on the musculature of the colon. The stool should be inspected daily, as whatever might be the improvement in the symptoms no marked change in the diet can be made with safety until the stool shows a form and consistency approximating normal. This occurs in from seven to twenty-one days, depending on the severity of the case.

Following this, the diet may be increased daily, the patient may be encouraged to take an increasing amount of exercise and the intervals between feedings lengthened to three hours.

After the symptoms have disappeared, and the stools have taken on normal form, if there is still a tendency to constipation, the laxative foods, that is, stewed fruits, rye bread, and honey, may be added to the diet. No yeast bread, meat or raw fruit, however, should be allowed for several weeks after the patient has seemingly regained his health. It is well, too, to advise the continuance of rather frequent feeding.

[The Editor commends the statements made, but believes that "spastic colon" is a better term to use. If colitis occur it is secondary to the irritation due to the

use of coarse foods and irritating cathartics. A management which will overcome the underlying neurotic condition of the patient and a soft creamy diet will usually be followed by recovery.—B.]

Sippy is quoted as believing that the diet is the key to all bowel affairs, and as emphasizing two things, namely, frequent feedings, at preferably two hour intervals, and abstinence from meat fiber and yeast bread. He believes that these food products, have an especially irritating effect upon a bowel that is in the least susceptible to irritation.

**Postural Treatment of Proctocolitis.** As an introduction to his discussion of this subject, A. A. Landsman<sup>7</sup> reviews the anatomy of the colon and emphasizes the fact that one should keep in mind its structure and position if proper treatment of disease in this organ is to be accomplished.

There are certain objections (and even danger) to forcing fluid into the large bowel with sufficient force to distribute it well into the lumen.

In order to overcome these objections, it has occurred to Landsman to utilize gravity and posture as aids in the distribution of smaller quantities of fluids throughout the large intestines by instillation. When fluid is to be introduced into the large bowel, the protoscope is passed and the patient inverted over the table in the usual way, so that he supports himself on his palms, his head resting on a cushion about two feet below the level of his buttocks. In this position, from 6 to 8 ounces of fluid are poured into the rectum, which then by gravity finds its way into the descending colon, as far as the spleno-colic flexure. If the patient is then directed to get back on the table and lie down on his right side, whatever fluid is present in the splenic end of the descending colon will trickle into the transverse portion, and even into the ascending portion, because the hepatic flexure is on a lower level than the spleno-colic flexure. If the head of the table is tilted slightly below the horizontal, there will be a tendency for more fluid to come down, which can then again be directed to the transverse colon by assumption of the right-sided posture. As the patient gets on his feet, any remaining fluid will natur-

(7) New York Med. Jour., May 17, 1919.

ally gravitate into the ascending colon, and even into the caput coli.

[If six or more ounces of fluid are injected by gravity, antiperistalsis and peristalsis will carry the fluid forward and backward in the colon without changing the posture of the patient. This antiperistalsis and peristalsis of the colon is physiologic and may be made use of in giving enemas. In inflammatory conditions or with organic obstruction of the colon this physiologic motor phenomenon of the colon fails.—B.]

This method has been employed by the author during the past two years at rectal clinics with results which are very encouraging even in old-standing cases. If there is pronounced ptosis of the transverse colon, and its relations have become much distorted, one can not accomplish all that is hoped for. However, as it is non-surgical and involves no risk, and offers a possibility of improvement, not cure, it is worth while to give it a thorough trial. The bowels soon begin to move more regularly, the bleeding diminishes, the discharge becomes less, burning and pruritus lose their intensity, the abdominal uneasiness disappears, the patient rests more comfortably, and begins to gain in weight. The choice of any particular medicament is not so important as the proper use of anything that may be selected, with this proviso, however, in atrophic cases, when the glandular structure is shrunken or destroyed, the secretions dried up, the mucosa cracked and fissured, remedies emulsified in an oily medium work best, whereas in the hypertrophic stage, when the tissues are relaxed, the discharge of mucus excessive, and the diarrhea troublesome, astringents and stimulants show the happiest results.

With the increase in the incidence of intestinal diseases, because of conditions brought about by the war, there is exposure to fresh avenues of infection and sources of morbidity which bring a new realization of the duties confronting the physician. Many such diseases caused by bacterial and protozoal infection injure the walls of the bowel by producing anatomic conditions which result in more or less permanent impairment of function long after the offending agent



has been expelled and are difficult to eradicate because they are hard to reach.

Postural treatment, according to the method of the author, as outlined in this article, seeks to overcome this, and should be given careful trial before surgical means to accomplish through and through irrigation are resorted to.

## DISEASES OF THE LIVER AND GALL-BLADDER

**Primary Sarcoma of the Liver!** On account of the rarity of this condition, J. S. Morros and W. H. McKinstry<sup>1</sup> record the following case.

The patient was a man, 42 years old, who presented himself at Queen Alexandria Military Hospital, Millbank, in a greatly emaciated condition. He had been in ill health for one year and suffered with pain in the stomach about half an hour after taking food, and had also a constant sense of discomfort during intervals between meals. Flatulence was a prominent feature, but there had never been any vomiting. There was no noteworthy constipation. There had been a steady progressive loss of weight.

On physical examination, the abdomen was found to be distended by a large smooth solid tumor extending from the costal margin to the brim of the pelvis. At its lower edge, a distinct fissure could be felt in the mid-line. Other physical findings aside from emaciation were of no great significance. The patient was not jaundiced.

At postmortem examination, when the abdomen was opened the liver was seen to have a mottled appearance and to be greatly enlarged, extending on both sides as low down as the iliac crests. The surface of the liver presented a large number of grayish white areas of new growth, some of which were about the size of a pea, while others were larger, umbilicated and slightly raised above the surface. The general "mottling" appeared to be due to the coalescence of these nodules forming large grayish patches, which were little if at all raised above the surface.

In the gastro-hepatic omentum, and in the mesentery, slightly enlarged lymphatic glands could be felt, and those about the head of the pancreas were particularly large and matted together. The liver weighed 14½ pounds and measured 23 inches in transverse diameter.

(1) Brit. Med. Jour., Sept. 20, 1919.

The gall-bladder and the bile duct were free from growth.

In the lungs there were numerous small white patches scattered over the surface. These were almost uniform in size, none of them being larger than a sago grain. Permission was not obtained to remove the brain.

When the liver was incised no abscess or cystic growth was to be found. The left lobe consisted almost entirely of a firm whitish growth with the exception of a small seam of liver tissue running across the surface near the lower anterior border. The growth extended to the right beyond the middle line and formed a greater part of the substance of the upper and anterior portions of the right lobe, penetrating backward to within two inches of the posterior surface. Small nodules separated from the main growth were scattered about in the remainder of the liver substance. The liver tissue was friable and pale and fatty in appearance. Pieces of the liver and of the lungs and some of the large lymphatic glands were excised, fixed and hardened in 10 per cent. formalin and sections cut and stained in the usual way with hematoxyline and eosine. On microscopic examination the growth from each of the above tissues were found to present the same histologic features, and a diagnosis of mixed-cell sarcoma of an alveolar type, primary in the liver, was made.

This growth was undoubtedly malignant and in view of the facts, first, that no evidence of a growth could be found after a most careful search in any of the other abdominal organs, and, secondly, the enormous size of the growth in the liver, the conclusion is reached that the tumor was a primary growth in the liver. Reference is made to the fact that very large tumors in the liver may be secondary to quite small growths in other organs, but here, no such growth could be found.

Primary sarcoma of the liver is a decidedly rare growth, as the following, brief, summary of the literature shows Hale-White, in 1890, recorded the fact that not a single case was met with at Guy's Hospital during the twenty years 1870-1899, both inclusive. Byrom Bramwell and Leith, in 1897, were able to collect only twenty-five cases, and they concluded that few of these

could be regarded as true examples. Vecchi and Guerini critically examined forty-five published cases and accepted only twenty-one as being undoubtedly primary sarcoma of the liver. Pepere also tabulated a list of forty-five cases, and Rolleston collected thirty-two cases in adults.

**Chronic Jaundice—Family Type.** Until a few years ago there was little published in regard to chronic jaundice of the family type. In describing the condition, J. I. Johnston,<sup>2</sup> of Pittsburgh, says the best term to describe the disease seems to be "splenomegaly with or in chronic, congenital, hemolytic jaundice." The disease is exceedingly rare and its pathology is not understood. It is true jaundice and not pigmentation of the skin, such as occurs in Addison's disease, or what is known as Gaucher's disease, which is also a splenomegaly. As one of the terms of its name expresses, it is a hemolytic and not an obstructive jaundice. The disease clinically is characterized by the striking, general chronic icterus, the large spleen, moderate anemia, good general health, and the possible history of more than one case in a family. The etiology of this disease is unknown, its pathology unexplained, and its entity recognition manifest by certain signs and symptoms, together with blood and urine changes.

There are two theories in regard to its manifest symptomatology, as well as its cytologic analysis. One is that there is an imperfect formation of the blood, and the other is that the normal cells are unstable or fragile and hemolysis follows due, possibly, to the presence of unsaturated fatty acids in the blood or reduced cholesterol, which is inhibitive normally. Some observers have suspected syphilis, and others that the condition might occur as a hereditary factor following tuberculosis. But these theories have failed.

A patient who presented this condition when he consulted Johnston was a man, 23 years old, an American by birth. His sister, aged 30 years, was seen by the author also, and presented exactly the same picture clinically, though no blood or urine examination was made on her. The histories of these two are practically the same, the

---

(2) Amer. Jour. Med. Sci., April, 1919.

man complaining only of a large leg ulcer, besides the jaundice, and the sister complaining of dysmenorrhea in addition to her icterus. They were otherwise well and lived and worked as other people do. The man had been jaundiced as long as he could remember, certainly from ten years of age. The jaundice had been of equal intensity during this time except when he had what was diagnosed as malaria, and during that time the jaundice became more intense. The family of which this patient was one, consisted of six living children, two of whom were suffering from chronic jaundice, including the patient.

By physical examination, the liver of this man was found slightly below the costal border, while the spleen was greatly enlarged and explained the distention of the left hemisphere of the abdomen. The urine presented no clinical abnormalities, save the presence of urobilin and the absence of bile. It was therefore considered an acholuric jaundice. The stools were normal in color. An examination of the blood revealed a moderate grade of secondary anemia, the hemoglobin being 45 per cent., red blood cells 3,150,000, white blood cells 11,000. The differential count was proportional. The polymorphonuclear count equalled 77 per cent. The blood Wassermann was negative. The patient was treated by Roentgen rays once a week with the hope of reducing the size of the spleen preparatory to a splenectomy. When last seen the spleen, after weeks of Roentgen-ray treatment, had been reduced to about two-thirds of its former size, with an increase in the jaundice and in hardness of the spleen. Johnston states that should the spleen be reduced to a manageable size, splenectomy will be urged upon the patient. The after-effects to splenectomy have been striking in some cases of this type of jaundice.

In the acquired type of jaundice the fragility of the cells has been corrected and their normal resistance to hemolysis has been restored, but in congenital family jaundice the cells never regain their normal resistance.

**Terminal Icterus of Tuberculous Subjects.** Two patients with complete jaundice just before death, were seen by P. Ameuille.<sup>3</sup> At necropsy complete destruction of all the hepatic cells was found—either from fatty de-



generation alone or associated with amyloid. As a rule, the liver in tuberculous individuals which seems most damaged is far from showing such complete destruction. Hence there is reason for attributing such cases to hepatic insufficiency. Moreover, they corroborate the view that the bile pigments are preformed in the blood, and eliminated by the liver which concentrates them.

### **The Spirochete of Infectious Jaundice in House Rats.**

The spirochete of infectious jaundice has been looked for in house rats in Chicago by A. Otterman,<sup>4</sup> working at the John McCormick Memorial Institute for Infectious Diseases. The rats studied in this work were captured in the basement of a hospital and of a medical college located in the City of Chicago. Thirty rats were used, a number of them being rather young. They were taken alive, killed, and one kidney aseptically removed at once. The kidney was then emulsified in salt solution, and the emulsion injected into the peritoneal cavity of a guinea-pig, one guinea-pig being used for each rat. The guinea-pig was then observed for at least three weeks, in most instances for one month.

The results of these observations were all negative. None of the guinea-pigs died and at no time did they show any symptoms of hemorrhagic jaundice.

The other kidney of the rat, together with the suprarenals, liver and spleen, the heart, lungs, and the testicles were treated according to Levaditi's silver method and examined for spirochetes.

The conclusions reached are as follows:

Spirochetes resembling those described as the cause of acute infectious jaundice were demonstrated in only two Chicago house rats of thirty examined (or 6.6 per cent.), indicating that the spirochetes probably are not present in a high percentage of such rats.

The spirochetes were demonstrated in material from the mouth and in tissue from the kidney.

Because of the presence of spirochetes in the mouth of rats it is possible that, at the time of the bite, organisms may be carried into the wound by the saliva or teeth, and the disease in this manner transferred directly from the rat to man.

(4) Jour. Inf. Dis., May, 1919.

**A Study on the Etiology of Cholecystitis and its Production by the Injection of Streptococci.** In 1914, Rosenow, by making cultures from the emulsified wall of the gall-bladder of selected patients, found streptococci in most instances, and reproduced cholecystitis in animals by injecting intravenously the freshly isolated organisms. The work recorded in the present report is similar to that of Rosenow, except that all gall-bladders removed in operations in the Mayo Clinic, regardless of the degree of pathologic changes, were cultured.

In this work, the author, R. O. Brown,<sup>5</sup> working in the Mayo Clinic, cultured altogether seventy gall-bladders and four gastric ulcers. Pathologic changes in the gall-bladders ranged from slight to marked thickening of the walls. In the gall-bladders showing slight changes 30 per cent. only yielded streptococci in contrast to 75 per cent. in those showing marked changes. Microscopic examinations of the gall-bladders failed to reveal bacteria when negative cultures were obtained, but bacteria were found consistently when cultures were positive.

Illustrative protocols from the animal experiments are presented in the original article.

In the summary it is stated that by making cultures of the emulsified tissues of gall-bladders or adjacent lymph glands, streptococci are found to be the chief microorganisms associated with cholecystitis. The direct etiologic relationship of the streptococci is established by their presence often in numbers proportionate to the degree of gross and microscopic changes, by their having elective affinities for the gall-bladders of animals and by the specific agglutinating power of the serum of the patient from whom isolated.

The elective affinity for the gall-bladder of animals of the strains from the tonsils indicates strongly that cholecystitis is commonly a blood-borne infection from a focal source.

**Recurring Cholecystitis.** In discussing the rôle of the cystic duct in recurring cholecystitis, J. E. Else<sup>6</sup> of Portland, Oregon, states that clinically the pathologic processes involving the cystic duct which serve as factors

(5) *Archiv. Int. Med.*, February, 1919.

(6) *Surg. Gynec. and Obstet.*, May, 1919.

in recurring cholecystitis may be divided into first, those that interfere with the lumen of the duct and thus cause stagnation of the gall-bladder making it a good incubator in which bacteria may grow; and second, those that harbor infectious organisms, which may pass up into the gall-bladder with the bile as it flows upward.

The anatomy and physiology of the duct are reviewed briefly in the original article. Under the heading of intrinsic obstruction, foreign bodies are placed first. Of these, gall-stones are the most frequent. Plugs of mucus sometimes obstruct, although probably not so frequently as was formerly supposed. Worms and echinococcus cysts have been reported as found in the cystic duct.

Edema, acute inflammation and chronic hyperplasia of the hiesterian valves of the cystic duct are placed as the second most common causes of obstruction to it.

Ulcers that produce the obstruction here are the result of pressure from stones, the action of infecting organism in the ducts, or the toxin of such organism and infection within the walls of the duct with sloughing of the infected areas into the lumen.

Some ulcers produce a considerable amount of induration and there results induration and spasm of the muscle which leads to interference with the lumen.

The author has not observed a primary carcinoma of the cystic duct. Of the intramural lesions that may produce obstructions here, strictures are considered first, and these, of course, are divided into congenital and acquired. The acquired usually follow injuries from gall-stones, the healing of ulcers or intramural infections. Under this heading are placed also localized infections, which may be due to organisms coming through the blood-stream, extension into the mucous glands, or by direct extension from within or without. Cysts or other enlargements of the mucous glands, hyperplasia of the muscles in the ducts or connecting tissue in its walls, and edema of the cystic duct, are other factors mentioned under this heading. Tumors are merely mentioned and not discussed.

Of the extrinsic causes of obstruction only two are mentioned: First, angulations due to adhesions, constricting bands of displacement of the ducts; and second,

pressure from tumors, enlarged glands, inflammatory and similar lesions.

The second chief division of the pathologic lesions found in the cystic duct is labeled as "processes which harbor infection." Here it is said that foreign bodies by interfering with the lumen, lowering the resistance to pressure or by the formation of pockets which hold bile, or the secretion of the mucosa or its glands, predispose to bacterial growth.

Obstructive lesions through producing a stasis predispose not only to bacterial growth, but also to the extension of the bacteria to the gall-bladder. Also, the mucosa of the cystic duct like that of the gall-bladder shows a predisposition to a fine villous growth in the presence of chronic irritation.

If ulcers are present they are a continuous source of infection. These are intrinsic lesions or the intramural lesions that come under this heading, those involving the mucous glands are the most important.

Under this heading there are mentioned simple infections within the glands, periglandulitis, intramural abscess, perforation of an intramural abscess into the duct or into the lesser omentum, or into the peritoneal cavity, chronic infection, intramural cysts, adenoma, and primary carcinoma.

Clinically, the obstructive lesions are classified according as they produce permanent complete obstruction, transitory complete obstruction, permanent partial obstruction, or transitory partial obstruction. In the obstructions the involvement of the gall-bladder may completely overshadow the cystic duct clinically.

The following conditions have been observed as the result of such obstruction: acute and chronic cholecystitis, hydrops, empyema, sclerosis and calcification.

Excluding the symptoms that come from the gall bladder involvement with the permanent complete obstruction, pain may be entirely absent, and when present is usually dull and never colic-like. Tenderness is present.

The transitory complete obstruction on the other hand is usually accompanied by pain which may be colic-like at first, but if the condition persists without an occasional remission or when due to a stone and the stone

does not pass on downward or becomes loosened, the pain soon loses its colic-like character. Infection is very frequently present in such instances.

Permanent partial obstruction is accompanied with tenderness and pain of a more or less dull character. In transitory partial obstruction tenderness is present and also pain varying with the degree of obstruction. Obstructive lesions by forming pockets or otherwise causing retention harbor infective organisms and thus predispose to infection of the rest of the biliary tract or through the blood-stream elsewhere in the body. The glands of the cystic duct become of importance clinically, first when they become infected, and second, when they become distended and encroach on the lumen of the duct.

The positive diagnosis of the lesions of the cystic duct are rarely made clinically or, with the exception of stones or other masses, upon close examination. In the majority of instances the microscope will be required. The clinical indications are for cholecystectomy.

**Chronic Echinococcus Obstruction of the Common Duct.** Speaking at the Paris Academy of Medicine, F. Dévé<sup>7</sup> said that in addition to obliteration of the common duct by calculi and cancer, there was another type but little known, due to obstruction by cysts or membranes from a hydatid cyst of the liver opening into the bile ducts. He had seen an example, and collected fifty others where the occlusion lasted from a month or two up to a year. The symptoms completely simulate a chronic calculous obstruction of the common duct. Differentiation is based on the ultimate appearance of urticaria, the presence of an hepatic tumor perceptible on palpation or recognized by the x-ray, by search for eosinophilia and the deviation of the complement. Passing the stools through a sieve often shows presence of characteristic débris of hydatid cysts.

This hydatid obstruction leads sooner or later to serious complications (angiocholitis, suppuration of the cyst, peritonitis, serious icterus, etc.). Hence early operation is essential; on some occasions drainage of the principal bile passage has sufficed for complete evacuation

---

(7) Prog. méd., Nov. 22, 1919.



of the cyst. From a theoretic standpoint, the primary cyst should be opened and drained directly.

**Regional Gastric Spasm in Cholelithiasis.** Lüdin<sup>8</sup> writes that in addition to the spasm localized at the pylorus or the cardia, three other types have been described: Circumscribed spasm, frequent in ulcer; total spasm, very exceptional; lastly the regional spasm which is rather infrequent, involves the prepyloric region especially—and gives a shadow (*x-ray*), easily mistaken for carcinoma. This last consists of a considerable and uniform narrowing of the horizontal portion and bounded by slightly undulating contours.

It is due to various causes: While operation or necropsy sometime shows the presence of gastric lesions—submucous phlegmons, burns from acids, uremic changes—at other times all lesions are absent, and we have to deal with biliary calculi, as in two patients seen by Lüdin.

In the first patient, the age, clinical signs—anachlorhydria, presence of lactic acid, a certain resistance in the pyloric region—led to suspicion of gastric cancer, which was apparently confirmed by the radiogram—a regular narrowing of the prepyloric region, with absent peristalsis. However, operation showed the region normal; on the other hand there was pericholecystitis, and a large stone in the gall-bladder. Recovery ensued after cholecystectomy.

In the second patient there was rapid emaciation, without clear-cut gastric symptoms. The same spasm, again evidenced by *x-ray*, led to exploratory operation, which again disclosed a biliary calculus and a healthy stomach. Cholecystectomy was followed by recovery.

Lüdin believes that the differentiation is one of the most delicate problems of gastric radiology. Repeated examination, if need be after administration of atropine, occasionally puts one on the right track by revealing in spasm a different image from the first; on the other hand, the marked contrast between the partly filled retracted portion, and the normally filled remainder is in favor of spasm. While the clinical picture should be appealed to,

(8) Cor.-Bl. f. Schweiz. Aerzte, Sept. 19, 1919.

it may prove misleading as in Case I, and the condition is only cleared up by exploratory laparotomy.

**Gumma of Liver, Causing Fatal Hemorrhage.** Details are given by Bouchet and Lamy<sup>9</sup> of a man who sought hospital care for albuminuria, disordered speech and weakness of intellect. Venereal disease was vehemently denied, and a Wassermann reaction was negative. There had been two slight "strokes" with transient vertigo, the only traces of which were a paralysis of the sixth nerve. In addition to exaggeration of reflexes, there was arterial hypertension with marked hypertrophy of the heart and slight albuminuria. The liver could not be felt. The general and mental symptoms became slowly aggravated, when one morning there was sudden onset of pain in the abdomen with syncope ending fatally in less than half an hour.

At necropsy, the kidneys were found small and sclerotic; the much enlarged heart weighed 600 gms. There were two fibroid plaques at the arch of the aorta. The peritoneal cavity was full of blood, and the lower surface of the liver presented an irregular laceration two inches wide; at first sight this seemed to be an aneurysmal sac especially as an arteriole appeared to act as a pedicle. Otherwise the liver was normal. On microscopic examination, however, instead of a ruptured aneurysm there were discovered many small gummas in the liver. The walls of the sac were similar in all respects to a gumma; there was rupture of an arteriole in an old sclerotic gumma. The syphilis here acted both by production of the gumma and the concomitant endarteritis. The cardiac hypertrophy and arterial hypertension played equally important rôles.

---

(9) Presse méd., Dec. 17, 1919.

## DISEASES OF THE PANCREAS

**Diagnosis of Diseases of the Pancreas.** Diagnosis of the diseases of the pancreas as presented by T. R. Brown,<sup>1</sup> of Baltimore, is preceded by a discussion of the anatomy and physiology of the gland. He then takes up in order the functional diagnosis, the etiologic factors involved, and the signs and symptoms derived from the usual methods employed in studying disease.

In making an examination of the stools from a patient suspected of having disease of the pancreas, the finding of bits of striped muscle or of thymus or other tissue rich in nuclei is of more significance than data obtained from the pure metabolic studies of nitrogen loss, especially if associated with a fatty stool, and in the absence of diarrhea, as of all the proteins these, perhaps, are more in need of pancreatic juice for complete digestion. The study of the duodenal contents for all three ferments, obtained by direct aspiration through an Einhorn or similar tube, is of unquestionable qualitative though more doubtful quantitative value.

Unquestionably data of great value may be derived from the study of the fat in the stools, especially in the absence of jaundice.

Diastase offers a singularly attractive field for study in this connection. In the opinion of the author, the quantitative estimation of the diastase in the stool is the easiest technically, has the most clean-cut end-reaction and is less open to criticism than any other method attempting to estimate quantitatively pancreatic function.

Etiologic factors in diseases of the pancreas of varying degrees of importance are first, catarrhal inflammation of the stomach and intestines, with its possibility of ascending infection of the pancreatic duct by various bacteria, notably the *B. coli* and certain cocci, or by the products of decomposition or inflammation. Second and of greater import is catarrhal inflammation of a gall-bladder or gall-duct, or presence of gall-stones. These

(1) Southern Med. Jour., August, 1919.

two, especially disease of the biliary system are by far the most important of the etiologic factors.

This last condition is easily understood if one remembers the anatomy of the biliary and pancreatic ducts.

Other etiologic factors are trauma, which possibly plays a rôle in the so-called apoplexy and in cysts of the pancreas; arteriosclerosis, leading to sclerosis of the pancreas; syphilis, which produces gumma in this organ; alcoholism as a possible factor in pancreatitis; and obviously various inflammations or neoplasms of the contiguous organs which may involve the pancreas by extension or by metastasis.

The symptoms of pancreatic disease are as a rule very vague, if chronic. Some of the symptoms are fullness, pressure, gas, pyrosis, sometimes nausea and vomiting, loss of appetite, etc., and these symptoms practically always simulate certain other acute abdominal conditions if the pancreatic disease is acute.

Pain when present is often uncommonly violent, sudden and colicky. Constipation is the rule, although diarrhea is sometimes found. Loss of weight and strength are often striking, especially in comparison with the paucity of other findings. Jaundice is very important and a persistent painless jaundice in persons who have passed middle life is very suggestive of carcinoma of the head of the pancreas or, much less frequently, of cirrhosis of the pancreas. A palpable tumor that is definitely shown to be pancreatic is very difficult to demonstrate, because of the location of the surrounding organs and the effect that they have on any attempt to palpate the pancreas.

The signs and symptoms are, in the main, not clear cut. Even with considerable experience, medical and surgical, a correct diagnosis is the exception rather than the rule. The picture of acute pancreatitis with its three stages—hemorrhagic, gangrenous and suppurative—is not one of infection or inflammation, but one of toxemia or shock, and high intestinal obstruction; and its profound prostration, thready pulse, lack of fever and absence of leukocytosis, sensitive epigastrium without muscle spasm, and the frequent previous history of gall-bladder or duodenal disease, especially the former, should make one suspect this condition more frequently

than is done. On the other hand, in cases with this history, not ending fatally and not operated upon, one should always be on the lookout for the symptoms of abscess or gangrene as late sequels.

In cases of chronic pancreatitis or cirrhosis of the pancreas, the history of the usual etiologic factors, the vagueness of the symptoms with their intractability to the usual methods of treatment, the increasing weakness of the patient without demonstrable cause, sometimes the deficiency of digestion of the various foodstuffs, notably the fats, as shown by stool studies after a Schmidt diet, should make one suspicious. A quantitative stool study often demonstrates—not the absence but a marked diminution of the diastase.

Cancer of the pancreas is usually of the scirrhus type, most often confined to the head of the organ and, if associated with jaundice, produces a rather characteristic picture—usually progressive jaundice often tending to a mahogany-brown color of the patient, with loss of weight and strength, often fatty stool, often alimentary glycosuria, usually distended gall-bladder, a point of real importance in differentiating it from obstructive jaundice due to gall-stone, often a previous history of gall-bladder disease.

Tuberculosis and syphilis of the pancreas are comparatively rare and present no characteristic symptom-complex.



## MISCELLANEOUS DISEASES

**Tropical Sprue in the United States.** There can no longer be any doubt of the existence of tropical sprue in the United States. While the majority of the cases are occurring in the Southern states, it is interesting to note that one of those studied by E. J. Wood,<sup>1</sup> came from New Hampshire. One was seen at Syracuse (a Porto Rico case) and one came to the Johns Hopkins Hospital. It is evident, therefore, that a familiarity with the cardinal symptoms of sprue would be helpful to many more of the profession than those of the South.

Sprue is characterized by three groups of symptoms, those of the mouth, the intestinal tract and the blood.

Most important of the symptoms of the mouth are those connected with the tongue which is inflamed and pink, with congested fungiform papillae, eroded patches and superficial cracks on the dorsum, and edges. The tongue in sprue is quite different from the tongue in pellagra. In the latter disease it will be found more pointed and not so flabby. In sprue it is very much paler than in pellagra. There is also, in sprue, an approach to the cobblestone appearance, which does not occur in pellagra.

The diarrhea in sprue is the most distinctive symptom. The bowel movements occur from midnight until about ten o'clock in the morning. There then occurs a cessation until the next day. If the cessation does not occur there will be a marked diminution in the afternoon and the early hours of the night. The bowel movements are very large, suggesting at once a pancreatic condition. The reaction is decidedly acid and there is much gas mixed with the feces. Examination of the feces reveals a large amount of fat, the stools are light in color, and give a positive reaction for hydrobilirubin. In addition to this failure in the utilization of fat and nitrogen there are other evidences of pancreatic insufficiency indicated

---

(1) Jour. Amer. Med. Ass'n, July 19, 1919.

by the thymus nucleus test and the Sahli glutoid-salol capsule test.

In describing the blood-picture the author states that in a large number of cases the color index is above 1.0; reference is made to a single instance in which the index was 1.66. The author believes that many cases of sprue have been called pernicious anemia. In sprue, there is most marked variation in the size of the red cells. There is found a decided preponderance of over-sized cells, as well as numerous dwarf cells. There also occurs poikilocytosis. When the blood smear is stained with any of the eosinates of methylene blue, there are found many cells that are very pale; stipple cells are rarely found; no nucleated red cells have been found in the author's experience.

Wood considers it worthy of emphasis that the remissions in sprue are as striking as those in pernicious anemia. The remarkable recurrence which is so often seen in pernicious anemia, even after years of quiescence, is also seen in sprue.

What the relation between the two diseases is, if any, remains to be seen, but it is not improbable that a more accurate study of sprue will shed light on many obscure corners in the study of pernicious anemia.

There is no longer an occasion to mention the confusion between sprue and pellagra. The matter should be dismissed with a word. If the sprue stool and tongue are considered, even in the light of an absence of the skin lesion there should be no confusion.

**An Outbreak of Scorbutus.** Some details connected with an outbreak of scorbutus among the inmates of an institution in Victoria, Australia, are reported by W. A. T. Lind.<sup>2</sup>

The institution at which this outbreak occurred was an asylum for the insane. Investigation showed the following:

All the patients infected were cripples and confined to bed or chair. The disease attacked both sexes with the same intensity and frequency. This was the first time the disease had appeared in the institution.

There had been no alteration in the dietary of the pa-

(2) *Med. Jour. Austral.*, Aug. 8, 1919.

tient for years. Other patients suffering from the same crippled condition and with the same food were unaffected. All the milk used in the institution was boiled before the patients consumed it. The food given to these hand-fed patients contained an excess of carbohydrates over the protein and it was all cooked. The timing of the onset in each ward suggested a contagious disease. The scurvy cleared up in the majority of the patients shortly after they received the following special dietary: Raw eggs, lime water, lemon juice and raw milk. A more liberal supply of vegetables, porridge and beef tea was given to all patients receiving invalid diet. The patients who died were examined postmortem, and showed extensive hemorrhage under the periosteum of the long bones and separation of the epiphyses. A careful study of the patients affected when considered in conjunction with the above facts, suggests to the author that in addition to the lack of certain vitamins, there may have been a contagious factor present in this epidemic. The facts concerning twelve patients are tabulated. Eight of these had swelling of the knees, legs or ankles. Ten suffered with sore mouth, and three had bleeding from the gums. Four died.

**Hyperpyrexial Heat-Stroke.** The object of this note is to suggest the adoption in heat-stroke countries generally of principles of prevention which proved to be successful in the hands of K. G. Hearne,<sup>3</sup> the author, in his work in Mesopotamia during a prolonged and very thorough test under varying conditions.

Hearne's observation on patients with heat-stroke point most conclusively to the belief that this condition is entirely due to the suppression of sweating which may be present for from one to forty-eight hours before the attack. With sweating suppressed, the bodily temperature tends to adjust itself in accordance with physical laws to the temperature of the atmosphere which may be 115° F. to 120° F. at the time, and even to rise higher, for it has been shown that a rise of bodily temperature produces increased respiratory and nitrogenous changes resulting in a **further** increase in internal bodily heat. The **processes continue** until when a temperature of

---

(3) Brit. Med. Jour., April 26, 1919.

about 108° F. or more is reached, sudden unconsciousness, delirium and convulsions occur, the result of the physical action of heated blood on the specialized brain cells. The clinical picture of the fully developed attack of heat-stroke is thus formed.

The suppression of perspiration is probably due to exhaustion of the sweating mechanism during several previous days of intensely severe weather and there is strong reason to believe that the defect is localized in the sweat glands themselves. Furthermore, large doses of diaphoretics are powerless to produce sweating when once suppression has set in.

The author cites his experience in preventing heat-stroke among hospital patients in Mesopotamia. The practice was to inspect the patients every hour during the hottest weather, and to detect in this way those who required preventive treatment. Any who were discovered to have a temperature of 103° F. with complete suppression were stripped and covered with a wet sheet. In cases in which the temperature had already risen dangerously high before discovery, a portable electric fan directing a current of air over the surface of the wet sheet was placed beside the bed. The evaporative process was greatly assisted by it. If it were possible to remove the patient to a ward which was artificially cooled to a suitable temperature, the individual cooling devices would, of course, be unnecessary.

By using these simple procedures, it is the belief of the author that hyperpyrexial heat-stroke is an absolutely preventable disease, the leading signs of onset being a hot dry skin which is typically harsh to the touch, and a raised body temperature. There is usually also frequency of micturition. These signs are present for from one to forty-eight hours before the attack, consequently ample warning is given. The position is simply this, that the patient having lost his natural means of heat dissipation, requires his bodily temperature to be artificially regulated for him during extremely hot weather until he again begins to sweat or until the heat waves abate. In the after-treatment following an actual attack of heat-stroke the tendency to relapses or hyperpyrexia are treated on exactly the same lines as for pre-

vention. The patient frequently does not regain his powers of sweating for days after the attack.

**The Treatment of Bilharziasis.** The use of tartar emetic in the treatment of bilharzial infection is discussed by Major Arthur Innes.<sup>4</sup>

His first statement is that tartar emetic as advised by J. B. Christopherson must be accepted as a positive cure of bilharzial infection. The patients treated under the author's directions are divided into two groups, the first consisting of twenty-six, and the second of thirty-six. This division is made chiefly on account of the time in which the patients were treated.

Of a third series of twenty-six patients, fourteen were discharged with the urine free of blood and ova, eleven were still infected, but were discharged on account of the influenza epidemic, after receiving doses of tartar emetic varying from 3 grains to 23 grains, and one died. All these patients were very heavily infected, having indeed been picked out at inspections for their unhealthy looks and found on examination to be infected by bilharzia. With the one exception all were returned to duty looking fit and were able to continue with their units after treatment.

The method of administration consists of the making up of tartar emetic with normal saline, with strength of  $\frac{1}{2}$  grain in 2 c. c. and sterilizing in an autoclave each time before injection. The dose varies from 5 grains in the first three or four injections to 15 grains in those given later. The author feels that as much as 25 grains may be given with safety. A 10 c. c. syringe is used to give the solution intravenously, and injection is never commenced until the blood of the veins has been seen in the barrel of the syringe and the plunger is always pulled back a little twice or thrice while the injection is being made to insure that the needle has not shifted out of the vein. Injections are always given fairly slowly, especially in cases in which vertigo is developed. By this means the number of such cases is diminished. Among complications mentioned, the cough is said to be extremely common, but is usually very slight. Vertigo

---

(4) Brit. Med. Jour., Sept. 13, 1919.



is much less common, but more troublesome. Vomiting is fairly common but never severe.

Of complications resulting from the injections themselves the only one to be expected, if reasonable attention be given to asepsis, is a little phlebitis at the seat of puncture of the vein. The results of the second series of thirty-six cases were as follows: Twenty-eight patients were discharged cured, no ova being found on careful examination of the urine, in one or two very little blood still existed, but it was surprising how in the vast majority from being almost pure blood, the urine became absolutely negative. Two patients were invalided from the service after receiving only 4 grains each. The first of these was invalided because of his very poor state of health, and the second because of the multiplicity of the intestinal infestations, ankylostoma, tenia, oxyuris, and a continued low fever. One, after receiving 16 grains was much affected with vertigo and treatment was stopped, although the urine contained more blood and mucus than was pleasing to the physician. This case, it is said, might be claimed as a cure, as no ova were found on the last examination. Four patients were discharged with ova still in the urine, after doses of 15, 13, 11 and 10 grains respectively, because of vomiting and vertigo. Of the twenty-eight persons discharged cured, fifteen were examined during the first and second month after they left the hospital, and in none were blood or ova found in the urine. The other thirteen were not available.

**Intravenous Infection of Antimony Tartrate (Tartar Emetic), in Bilharziasis.** In a summary of recent advances in connection with the disease of bilharziasis, it is stated that in 1915 Leiper worked out a complete cycle of development of the bilharzial worms, giving a connected story of their life-history. He found that the non-eyed, bifid-tailed cercariae, characteristic of the genus of two genera of snails, *Bullinus contortus* and *Planorbis boissyi*. These snails were shown to harbor two different species, *Bilharzial haematobia*, characterized by a terminal-spined ovum, and *Bilharzia mansoni*, characterized by a lateral spined ovum.

This bit of information is given as an introduction to

a record of intravenous injection of antimony tartrate (tartar emetic) in bilharziasis by Frank E. Taylor.<sup>5</sup> He treated ten patients successfully by this method. In all the cases the solutions used were made by dissolving the tartar emetic in freshly distilled sterile water, 1 grain in 6 c. c., and then sterilized by autoclaving for one hour. At first the injections were administered every two days with a maximum dose of 2 grains, while on the later cases, the patients were worked up to doses of 3 grains twice a week. No serious drawbacks, no marked complications and no severe reactions followed the injections. With one exception, all the patients were troubled with irritation of the pharynx and a spasmodic outburst of coughing, either during or after the injection, usually just at the end of administration. In four cases stiffness and cramp of the muscles of the neck and shoulder girdle were complained of. Gastro-intestinal symptoms were fairly frequent comprising nausea in three instances, vomiting, usually once only, in four, and slight diarrhea in three. Headache was noted in two patients. There was induration at the seat of the injection in two cases. Pyrexia to 103° F., slight giddiness, pains in the body, general pruritus and loss of weight were noted in one case each.

The immediate results were very striking and comprised a rapid disappearance of the blood and ova from the urine, disappearance or mitigation of hypogastric and perineal pain and pains in micturition, improvement in anemia, gain of weight, and a quite striking improvement in general appearance and a feeling of well-being. The remote results can not be discussed owing to the short time elapsed.

Attention is called to the fact that Sir Leonard Rogers has noted the occasional danger from the toxicity of tartar emetic intravenously, and has done the pioneer work in searching for equally efficient but less toxic forms of antimony. He found colloid antimony sulphide effective in smaller doses, being retained in the blood longer than the soluble tartrates of antimony, and concludes that it appears a distinct advance on soluble antimony tartrate.

(5) *Lancet*, Aug. 9, 1919.

## INDEX.

- Abdominal complications of influenza, 114
- Acid base equilibrium of human system, regulation of, 17
- Achylia gastrica, 516
- Acidosis and errors of metabolism, 22
- in diabetes, 21, 445
- Actinomycosis of heart, 346
- Adrenal: See Suprarenal
- Amebiasis: See also Dysentery
- Amebiasis, chronic intestinal, mixed treatment of, 204
- Animals, relation of human la grippe to diseases of, 65
- Anaphylactic death in asthma, 276
- Anemia, 383
- pernicious, basal metabolism following transfusion in, 387
- pernicious, chemistry of, 385
- pernicious, diagnosis and prognosis in, 383
- pernicious, duration of remission in, 384
- Aneurysm, aortic, treated by wiring and electrolysis, 356
- Angina pectoris, 365
- Anthrax, 243
- fatal case of, 247
- human, treatment of, 243
- local use of serum in, 245
- Antibody production, relation between feeding yeast and, 14
- Antigen, non-specific, hemoprotein, in arthritis, 174
- Antimony, intravenous injection of, in filariasis, 381
- tartrate, intravenous injections of, in bilharziasis, 609
- Aorta, abdominal, rupture of, 364
- disease of, 359
- disease of, in soldiers, 362
- Aortic stenosis and mitral insufficiency, differential diagnosis of, 318
- Aortitis, syphilitic, 359
- Appendicitis, chronic, value of transitional leukocytosis in diagnosis of, 524
- Arkansas rice fields, control of malaria in, 182
- Arthritis and meningococcus rheumatism, 169
- and rheumatism, 165
- meningococcus, 172
- non-specific, hemoprotein antigen for treatment of, 174
- Ascaris lumbricoides, pulmonary infection with, 285
- Asthma, anaphylactic death in, 276
- bronchial, pollen treatment of, 269
- bronchial, review of, 274
- bronchial, vaccine treatment of, 266
- horse, following blood transfusion, 265
- Auricular fibrillation, digitalis in treatment of, 335
- flutter, treatment of, 334
- Bacilli: See also Bacillus
- Bacilli, tubercle, human, bovine and avian, attenuation of, 30
- typhoid, fate of, in immune animals, 191
- Bacillus, Flexner-Y, recovered from blood during life, 382

- influenzae, endocarditis due to, 342  
 influenzae, immunity reactions to, 94  
 influenzae in normal throat, 77  
 influenzae in paranasal sinus infection, 76  
 influenzae, microorganisms resembling, as pus producers, 66  
 of Spanish influenza, 71  
 Pfeiffer, in influenza, 67  
 Pfeiffer, in measles, 231  
 Bacteria, fate of, introduced into upper air passages, 263  
 Bacterial protein injections in influenza, 108  
 Bacteriology of epidemic influenza and pneumonia, 70  
 of pneumonia, antemortem and postmortem, 126  
 Banti's disease, 388  
 Benzyl benzoate treatment of protozoal dysentery, studies of, 208  
 Bilharziasis, intravenous injection of antimony tartrate in, 609  
 treatment of, 608  
 Blood and blood-making organs, disease of, 371  
 and urine, chemistry of, 458  
 changes in, immediately following transfusion, 376  
 citrated, cause of reactions following transfusion of, 371  
 examinations in pulmonary tuberculosis, 34  
 excess of cholesterol in, in nephritis, 487  
 from measles patients, insusceptibility of man to inoculation with, 228  
 in urine, 464  
 plasma chlorides and renal function, 472  
 pressure and prognosis, 355  
 pressure: See also Hypertension  
 pressure, study of, in 150 patients, 351  
 recovery of Flexner-Y bacillus from, during life, 382  
 spirochetes in, in trench fever, 227  
 transfusion, 371, 376, 377  
 transfusion, horse asthma following, 265  
 transfusion in pernicious anemia, effect of, on basal metabolism, 387  
 transfusion, methods, 378  
 vessels and heart, diseases of, 310  
 Botulism, 563  
 Bradycardia, rare types of, 331  
 Brain complications of mumps, 234  
 Breast milk, typhoid fever transmitted through, 192  
 Bright's Disease: See Nephritis  
 Bronchi and upper air passages, diseases of, 263  
 spirochetosis of, 281  
 Bronchial Asthma: See Asthma  
 Bronchiectasis, 278  
 and pulmonary tuberculosis, differentiation of, 278  
 lung abscess and pulmonary tuberculosis, differentiation of 303  
 Bronchopneumonia: See also Pneumonia  
 Bronchopneumonia following measles, 145  
 influenzal, vaccine therapy in treatment of, 106  
 Bulimia, 522  
 Cardioresenal diseases, diet in, 489  
 Cardiovascular defective, 331  
 Catarrh, gastric, mucous, 518  
 Cecum, gumma of, 582  
 Cerebrospinal fever: See Meningitis  
 Cholecystitis, study of etiology of, and its production by injection of streptococci, 595  
 recurring, 595

- Cholelithiasis, regional gastric spasm in, 599
- Cholera, etiology of, 240  
treatment of, 242
- Cholesterin, excess of, in blood in nephritis, 487
- Circulatory system, energy index of, 350
- Clinical diagnosis as compared with necropsy findings, 10  
diagnosis, errors of omission in, 10
- Colds, etiology and treatment of, 120  
pathology of, 122
- Colic, renal, diagnosis of, 479
- Colitis, spastic, 584
- Complement-fixation test in diagnosis of tuberculosis, 35, 37
- Contagion, 27
- Death, anaphylactic, in asthma, 276
- Dengue and its relationship to yellow fever, 226
- Desiccation, influence of, on human, normal isohemagglutinins, 12
- Diabetes insipidus and the pituitary gland, 434  
mellitus, 445  
mellitus, control of acidosis in treatment of, 445  
mellitus, diet in, 445, 453  
mellitus, results in modern treatment of, 450  
mellitus, treatment of, in children and adolescents, 454
- Dibothriocephalus latus, the broad tapeworm, 568
- Diet in diabetes, 445, 453  
in renal and circulatory disease, 489  
scurbic, effect of, on suprarenals, 430
- Diets restricted, effect of, on gastric secretion and motility, 503
- Digitalis, action of, on rheumatic heart, 337  
in cardiac cases with regular pulse rate, 340
- Diseases, chronic, malignant, treatment of, 7
- Diverticulum of duodenum, 527
- Drug treatment of tuberculosis, 57
- Duct, common, chronic echinococcus obstruction of, 598
- Ductless glands, diseases of, 396
- Duodenal alimentation in peptic ulcers, 552  
and gastric ulcer, 528  
and gastric ulcer, diagnosis of, 531, 535  
and gastric ulcer, perforated, 555  
ulcer and ptosis of duodenum, 542
- Duodenum, ulcer and ptosis of, 542  
diverticulum of, 527
- Dysentery: See Also Amebiasis
- Dysentery, 200  
amebic, chronic, treatment of, with double iodide of emetine bismuth, 207  
amebic, epidemiology and treatment of, 203  
amebic, in Britain, 201  
amebic, treatment of carriers of, 211  
bacillary and amebic, 200  
bacillary, vaccine therapy of, 205  
in British army in East, 202  
protozoal, studies on treatment of, with benzyl benzoate, 208  
recovery of Flexner-Y bacillus from blood of patient during life, 382
- Echinococcus infection of pericardium secondary to hydatid cyst of heart, 348  
obstruction, chronic, of common duct, 598
- Electrocardiograph, value of, 312
- Emetine- bismuth treatment of dysentery, 207



- Empyema, postpneumonic, management of, 295  
   study of hemolytic streptococci in throat in, 302  
   treatment of, 292, 295  
 Encephalitis, influenzal, 117  
 Endameba, new form of,  
 Endocarditis due to influenza bacillus, 342  
   meningococcus, 341  
 Energy index of circulatory system, 350  
 Epinephrine, effect of, on basal metabolism in cases of irritable heart, 328  
   effect of, on electrocardiogram in irritable heart, 330  
   injections in irritable heart, effects of, 325, 328, 330  
   test for determining relation of neurocirculatory asthenia to hyperthyroidism, 422  
 Errors of omission in clinical diagnosis, 10  
 Exophthalmic Goiter: See Goiter And Hyperthyroidism  
 Exudates, pneumonic, biochemical studies of, 124  
  
 Face mask in prevention of droplet infection, 27  
 Filariasis, intravenous injection of antimony in, 381  
  
 Gall-bladder, and liver, diseases of, 590  
 Gas, mustard, inhalation of, pathology, 289  
 Gastric and hepatic disorders, differentiation of, 500  
   mucous catarrh, 518  
   secretion and motility, effect of restricted diets on, 503  
   spasm, regional, in cholelithiasis, 599  
   and duodenal ulcer, 528  
   ulcer and duodenal ulcer, frequency of diagnosis of, 535  
   ulcer and duodenal ulcer, perforated, 555  
   ulcer, diagnosis of, 528, 531, 539, 543  
   ulcer, duodenal alimentation in, 552  
   ulcer, treatment of, 549  
   ulcer, x-ray diagnosis of, 539  
 Gastroduodenal ulcer, diagnosis of, 531, 535  
 Gastro-intestinal diagnosis, x-ray in, 497  
   diseases, diagnosis of, 492, 497  
   disorders and therapeutics, 505  
   syndromes found in pulmonary tuberculosis, 45  
   tract, diseases of, 492  
 Gaucher's disease in adults, 390  
 Gelatine injection, fatal tetanus after, 249  
 Glycemia, renal, 474  
 Goiter: See also Thyroid  
   Goiter, exophthalmic, course and prognosis of, 410  
   exophthalmic, thymus in, 414  
   in young men, 398  
   prevention of, 417  
   simple, 405  
 Granuloma, Hodgkin's mediastinal, 258  
 Gumma of cecum, 582  
   of liver, 600  
  
 Heart, actinomycosis of, 346  
   and blood-vessels, diseases of, 310  
   and veins, extensive thrombosis of, 348  
   auricular fibrillation, digitalis in treatment of, 335  
   auricular flutter and its treatment, 334  
   complications of influenza, 111, 113  
   defective, 331  
   disease and distress, left scapular pain and tenderness in, 321  
   disease, electrocardiograph in diagnosis of, 312  
   disease, new diagnostic methods in, 310  
   disordered action of, 324  
   disordered action of and tuberculosis, 51

- function in test marches, 311  
hydatid cyst of, with secondary echinococcus infection of pericardium, 348  
in influenza, 111, 113  
irritable, effect of epinephrine on electrocardiogram in, 330  
irritable, pulmonary tuberculosis in soldiers with, 50  
patients with regular pulse rate, digitalis in, 340  
rheumatic, effect of digitalis on, 337  
stimulants, prolonged use of, 355
- Heat-stroke, hyperpyrexial, 606
- Hematemesis, significance and treatment of, 513
- Hematogenous infections of the kidney, 477
- Hematuria, clinical significance of, 464  
etiology of, 466
- Hepatic: See Liver
- Hodgkin's disease, treatment of, 440  
granuloma, mediastinal, 258
- Hookworm infection, 574  
treatment of, 575, 577, 579  
treatment of, in soldiers, 580
- Hydatid cyst of heart with secondary echinococcus infection of pericardium, 348
- Hypertension as observed in 150 patients, 351
- Hyperthyroidism: See also Goiter and Thyroid
- Hyperthyroidism, 408  
basal metabolism in, 423  
in recruits, 400  
relation of neurocirculatory asthenia to, as determined by effects of injection of epinephrine, 422  
symptoms of, in exhausted soldiers, 402  
without exophthalmos, 418
- Hypophysis and diabetes insipidus, 434
- Hypothyroidism and myxedema, 415
- Icterus: See also Jaundice
- Icterus, terminal, of tuberculous subjects, 593
- Immunity, acquired, to influenza, 93
- Indigestion, causes of, 506
- Infecting agent in influenza, 69
- Infection, droplet, and its prevention by face mask, 27
- Infectious diseases, 27  
diseases, intravenous injection of peptone in, 25
- Influenza: See also La Grippe
- Influenza, acquired immunity to, 93  
and pneumonia, prophylactic inoculations in, 100, 101  
and tuberculosis, 115  
bacillus, immunity reactions to, 94  
bacillus in paranasal sinus infection, 76  
bacillus vaccine, effect of, as prophylactic, 105  
bacillus, pus-producing microorganisms resembling, 66  
bacterial protein injections in, 108  
cardiac complications of, 111, 113  
composition of mixed vaccine for use in prophylaxis of, 101, 102  
encephalitis due to, 117  
epidemic, and pneumonia, bacteriology of, 70  
epidemic at Camp McArthur, 98  
epidemic, clinical observations on, 95  
epidemic, effect of, on skin sensitiveness to tuberculin, 64  
etiology of, 84  
filter-passing virus of, 80  
gross pathology of, 88  
heart in, 111, 113  
infecting agent in, 69  
inter-abdominal complications of, 114  
nature and mode of action of pathogenic agent in, 75

- paralysis of soft palate due to, 118  
 pathologic anatomy and bacteriology of, 85  
 Pfeiffer bacillus in, 67  
 pleural effusion in, 89  
 pneumonic, 63  
 prophylactic vaccination against, 100, 101, 104, 106  
 prophylaxis of, 118  
 purulent pneumococcus meningitis in, 116  
 serum reactions in, 99  
 serum studies on etiology of, 79  
 Spanish, bacillus of, 71  
 suprarenal involvement in, 91  
 transmission of, 73  
 Inoculations, prophylactic, in influenza and pneumonia, 100, 101  
 Intestinal obstruction, 580  
   obstruction and kidney function, 469  
   parasites, 566  
 Intestines, protozoal infections of, 566  
 Intravenous injection of foreign protein, 24  
 Isohemagglutinins, human, normal, influence of desiccation on, 12  
 Jaundice, chronic, familial, 592  
   infectious, spirochete of, in house rats, 594  
   terminal, in tuberculosis, 593  
 Kidney and circulatory diseases, diet in, 489  
   colic, diagnosis of, 479  
   diseases of, 458  
   effect of foreign protein on, 484  
   function and blood plasma chlorides, 472  
   function influenced by intestinal obstruction, 469  
   glycosuria, 474  
   hematogenous infections of, 477  
   infections, study of, 475  
   tuberculosis, unilateral, importance of early diagnosis of, 481  
 La Grippe: See also Influenza  
 La grippe, human, relation of, to certain diseases of animals, 65  
 Lambliæ enteritis, 569  
 Leptospira-icteroides, 222  
   in blood and urine of yellow fever patients, 224  
 Leukemia, acute, and so-called mediastinal leukosarcomatosis (Sternberg), 259  
 Leukocytosis, transitional, value of in diagnosing chronic appendicitis, 524  
 Leukosarcomatosis (Sternberg), mediastinal, and acute leukemia, 259  
 Liver and gall-bladder, diseases of, 590  
   and gastric disorders, hepatic test for differentiation of, 500  
   gumma of, causing fatal hemorrhage, 600  
   primary sarcoma of, 590  
 Lung abscess, bronchiectasis, and pulmonary tuberculosis, differentiation of, 303  
 Lungs and pleurae, diseases of, 285  
   and suprarenals, mesothelioma of, 428  
   infection of, with ascaris lumbricoides, 285  
   margin of safety in circulation in, 289  
   pathology of mustard gas inhalation, 287  
 Lymphatic glands, diseases of, 440  
 Malaria, 176  
   carriers, pepsin-quinine mixture in treatment of, 180  
   control of, in Arkansas rice fields, 182  
   in British army in Palestine, 184

- in Macedonia during the war, 187  
prophylactic use of quinine in, 190  
studies on malaria control, 176  
Wassermann reaction in, 181  
Malignant diseases, chronic, treatment of, 7  
epithelial growths of thyroid, 425  
Mask, face, in prevention of droplet infection, 27  
Measles, 228  
followed by bronchopneumonia, 145  
etiology of, 233  
occurrence of Pfeiffer bacillus in, 231  
patients, insusceptibility of man to inoculation with blood from, 228  
Mediastinum, diseases of, 258  
Hodgkin's granuloma of, 258  
Medicine, progress of, 7  
Meningitis and meningococcus infections, 146  
at Army camp, clinical study of, 150  
clinical picture of, 146  
meningococcus, among Chinese civilian population, 157  
Meningococcus at Camp Lee, statistics of, 161  
meningococcus, ward epidemic of, 156  
pneumococcus, 159  
pneumococcus, purulent, in influenza, 116  
streptococcus, acute, with recovery, 162  
Meningococcus arthritis, 172  
endocarditis, 341  
infection, extrameningeal, 149  
infections and meningitis, 146  
infections, determination of type of, 148  
meningitis among Chinese civilian population, 157  
meningitis at Camp Lee, statistics of, 161  
meningitis, ward of, 156  
pneumonia, 127  
rheumatism and arthritis, 169  
serum, from different sources, variation in strength of, 160  
Mesothelioma of both suprarenals and lungs, 428  
Metabolism, basal, in hyperthyroidism, 423  
diseases of, 445  
errors of, and acidosis, 22  
Mitral stenosis and aortic insufficiency, differential diagnosis of, 318  
Mosquitoes and yellow fever, 225  
Mumps, 234  
cerebral complications of, 234  
in U. S. Navy hospital, 236  
Mustard gas inhalation, pathology of, 287  
Myxedema and hypothyroidism, 415  
Nasopharynx, persistence of poliomyelitis virus in, 163  
Necropsy: See also Post-mortem  
Necropsy findings compared with clinical diagnosis, 10  
Nephritis, acute unilateral, hematogenous, 488  
early, chronic, interstitial, uric acid in, 486  
excess of cholesterin in blood in, 487  
Neurocirculatory asthenia, relation of thyroid to, 420  
asthenia, relation of, to hyperthyroidism as determined by injection of epinephrine, 422  
Nutrition, physiology of, 507  
Pain and tenderness in heart disease, localization of, 321  
Palate, soft, influenzal paralysis of, 118  
Pancreas, diagnosis of diseases of, 601  
diseases of, 601

- Panophthalmitis in meningococcus arthritis, 173  
     in meningococcus pneumonia, 128  
 Paralysis, influenzal, of soft palate, 118  
 Paratyphoid and typhoid fevers, 191  
     infections of pleurae, 292  
     third form of, 199  
 Pepsin-quinine mixture in treatment of malaria carriers, 180  
 Peptic ulcer, diagnosis of, 528  
     ulcers, duodenal alimentation in, 552  
 Peptone, intravenous injection of, in infectious diseases, 25  
 Pericarditis as complication of pneumonia, 344  
 Pericardium, secondary echinococcus infection of, in hydatid cyst of heart, 348  
 Pertussis, 237  
     resorcin in, 237  
     treatment of, 237  
 Physical reconstruction applied in treatment of pulmonary tuberculosis, 59  
 Pineal-gland, functions and uses of, 439  
 Pituitary Gland: See Hypophysis  
 Pleurae and lungs, diseases of, 285  
     paratyphoid infections of, 292  
 Pleurisy, serofibrinous, treatment of, with artificial pneumothorax, 309  
 Pneumococcus meningitis, 159  
     meningitis, purulent, in influenza, 116  
 Pneumonia: See also Bronchopneumonia  
     Pneumonia, 124  
         and epidemic influenza, bacteriology of, 70  
         and influenza, prophylactic inoculations in, 100, 101  
         and its complications, 130  
         antemortem and postmortem bacteriology of, 126  
         biochemical studies of exudates in, 124  
         influenzal, and influenza, 63  
         influenzal, non-specific proteins in treatment of, 110  
         lobar, serum treatment of, 143  
         meningococcus, 127  
         pericarditis complicating, 344  
         serum treatment of, 138, 140, 143  
         Type I treated with anti-pneumococcus serum, 138  
         treatment of, 136  
         vaccination in prophylaxis of, 134  
     Pneumoperitoneum, 512  
     Pneumothorax, artificial, in treatment of serofibrinous pleurisy, 309  
     Poliomyelitis, 163  
         persistence of virus of, in nasopharynx, 163  
     Pollens in treatment of bronchial asthma, 269  
     Postmortem: See also Necropsy  
     Proctocolitis, postural treatment of, 587  
     Protein, foreign, effect of, on kidney, 484  
         foreign, intravenous injection of, 24  
         injections, bacterial, in influenza, 108  
         therapy, 24  
     Proteins, non-specific, in influenzal pneumonia, 110  
     Protozoal infections of the intestines, 566  
     Pus-producing organisms resembling influenza bacillus, 66  
     Quinine pepsin mixture in treatment of malaria carriers, 180  
         prophylactic use of, in malaria, 190  
     Rabies and its treatment, 253  
     Radiation in malignant conditions, 8



- Reaction, Wassermann, in malaria, 181
- Renal: See Kidney
- Resorcin in whooping cough, 237
- Respiratory tract, upper, and bronchi, diseases of, 263  
upper, fate of bacteria introduced into, 263
- Rest in treatment of tuberculosis, 53 •
- Rheumatism, acute, 167  
and arthritis, 165  
in light of modern research, 165  
meningococcus, and arthritis, 169
- Roentgen-ray diagnosis of gastric ulcer, 539  
diagnosis of pulmonary tuberculosis, 42  
in gastro-intestinal diagnosis, 497  
in malignant tumors, 9
- Sand-fly fever, 226  
fever and its relationship to dengue, 226
- Sarcoma of stomach, 558  
primary, of liver, 590
- Scorbutic diet, effect of, on suprarenals, 430
- Scorbutus, outbreak of, 605
- Serum: See also Vaccine
- Serum, antimeningococcus, from different sources, variation in strength of, 160  
reactions in influenza, 99  
studies on etiology of influenza, 79  
treatment of anthrax, 245  
treatment of pneumonia, 138, 140, 143  
treatment of typhoid, 193
- Sinus infection, paranasal, influenza bacillus in, 76
- Skin sensitiveness to tuberculin, effect of epidemic influenza on, 64
- Smallpox, vaccination by injection, 238
- Sodium bicarbonate in production of tetany, 23
- Soldiers, pulmonary tuberculosis among, 49  
with irritable heart, pulmonary tuberculosis in, 50
- Spirochete of infectious jaundice in house rats, 594
- Spirochetes in blood in trench fever, 227
- Spirochetosis, bronchial, 281
- Spleen, diseases of, 388
- Sprue, tropical, in United States, 604
- Status lymphaticus, 427
- Stomach: See also Gastro-intestinal
- Stomach, sarcoma of, 558  
syphilis of, 562
- Streptococci, hemolytic, in throat in empyema, study of, 302  
in production of cholecystitis, 595
- Streptococcus meningitis, acute, with recovery, 162
- Suprarenal involvement in influenza, 91
- Suprarenals and lungs, mesothelioma of, 428  
diseases of, 428  
effects of scorbutic diet on, 430  
traumatic and tuberculous lesions of, 433  
tuberculosis of, without bronzing, 432
- Syphilis of aorta, 359  
of liver, 600  
of stomach, 562
- Tachycardia and test marches, 311
- Tapeworm, broad, 568
- Tartar emetic in bilharziasis, 609
- Test, complement-fixation, in diagnosis of tuberculosis, 35, 37
- Tetanus, fatal, after injection of gelatine, 249

- long incubation period in, 248
- treatment of, 250
- Tetany produced by sodium bicarbonate, 23
- Thoracic aspiration preliminary to vomiting in man, 513
- Throat, normal, influenza bacillus in, 77
  - study of hemolytic streptococci in, in empyema, 302
- Thrombosis, extensive venous and cardiac, 348
- Trench fever, spirochetes in blood in, 227
- Thymus, diseases of, 427
  - rôle of in exophthalmic goiter, 414
- Thyroid: See also Goiter
- Thyroid abnormalities in young men, 398, 400
  - diseases of, 396
  - function, method of testing, 396
  - malignant epithelial growths of, 425
  - relation of, to neurocirculatory asthenia, 420
  - studies of in soldiers at Camp Lewis, 399
- Tumors, malignant, of thyroid, 425
  - malignant, treatment of, 7
- Tubercle Bacilli: See Bacilli
- Tuberculin, effect of epidemic influenza on skin sensitiveness to, 64
- Tuberculosis, 30
  - active, 47
  - and disordered action of heart, 51
  - and influenza, 115
  - and trauma of the adrenals, 433
  - biologic method of ascertaining presence of active foci of, 48
  - complement-fixation test in, 35, 37
  - conjugal, 32
  - drug treatment of, 57
  - early diagnosis of, 42
  - pulmonary, blood examinations in, 34
  - pulmonary, and bronchiectasis, differentiation of, 278
  - pulmonary, bronchiectasis, and pulmonary abscess, differentiation of, 303
  - pulmonary, chronic, diagnosis of, 39
  - pulmonary, diagnostic value of x-ray examination in, 42
  - pulmonary, gastro-intestinal syndromes in, 45
  - pulmonary, in soldiers, 49
  - pulmonary, in soldiers with irritable heart, 50
  - pulmonary, incipient, new diagnostic sign in, 38
  - pulmonary, organisms of secondary infection in, 33
  - pulmonary, physical reconstruction in treatment of, 59
  - renal, unilateral, importance of early diagnosis of, 481
  - of the adrenals without bronzing, 432
  - rest in treatment of, 53
  - terminal icterus in, 593
- Typhoid among American troops in England, 197
  - and paratyphoid fevers, 191
  - bacilli, fate of, in immune animals, 191
  - fever after prophylactic inoculation, 194
  - fever, serotherapy of, 193
  - fever transmitted through breast milk, 192
- Uric acid in early, chronic interstitial nephritis, 486
- Urine and blood, chemistry of, 458
  - clinical significance of blood in, 464
- Vaccination, prophylactic, against pneumonia, 134
- Vaccine: See also Serum
- Vaccine, influenza bacillus, as prophylactic, effect of, 105
- Therapy: See also Vaccines

- therapy in influenzal broncho-  
pneumonia, 106  
treatment of bacillary dysen-  
tery, 205  
Vaccines: See also Vaccine  
Therapy  
Vaccines as prophylactic  
against influenza in British  
troops, 106  
in bronchial asthma, 266  
in prophylaxis of influenza,  
100, 101, 102, 104, 106  
mixed, in prophylaxis of in-  
fluenza, 101, 102  
Vermicides in hookworm, 575  
Virus, filter-passing, in certain  
diseases, 15  
filter-passing, of influenza, 80  
Vomiting in man, thoracic as-  
piration preliminary to,  
513
- Whooping Cough: See Pertussis
- Yeast, feeding with, and anti-  
body production, 14
- Yellow-fever, 218  
acquired immunity to, 220  
clinical features and patho-  
logic changes in, 218  
Leptospira icteroides in, 222  
mosquitoes in relation to, 225  
patients, Leptospira icter-  
oides in blood and urine  
of, 224  
patients, relation of blood  
serum of, to infecting or-  
ganism, 221  
search for organism of, in  
wild animals, 224  
symptomatology and path-  
ology of, 219  
transmission of, 218

## INDEX OF AUTHORS.

- Abram, J. H., 292  
Addis, T., 420  
Allen, F. M., 474  
Ambrose, L., 193  
Ameuille, P., 593  
Amoss, H. M., 163  
Antz, H. W., 33  
Asuzano, M. A., 208  
Aub, J. C., 423  
Auge, 65  
Barach, J. H., 350  
Barbié, 65  
Barrier, E., 181  
Barron, M., 287  
Barsky, J., 385  
Bass, C. C., 176  
Bashford, E. F., 15, 80  
Bassler, A., 531  
Bayliss, W. M., 507  
Beaven, P. W., 91  
Bell, E. T., 484  
Benjamin, J. E., 310  
Bergoignan, P., 489  
Berkeley, W. N., 439
- Billings, F., 59  
Birge, E. G., 126  
Bloomfield, A. L., 64, 95, 263  
Boas, E. P., 422  
Boettiger, C., 130  
Boggess, W. F., 418  
Bohan, P. T., 514  
Bonn, H. K., 425  
Bouchet, 600  
Boughton, T. H., 276  
Bowman, F. B., 84  
Boyd, F., 184, 202  
Boyd, J. S. K., 383  
Boyd, W., 458  
Bradford, J. R., 15, 80  
Bram, I., 410, 417  
Braud, S. F., 145  
Brittingham, H. H., 371, 387  
Brooks, C., 175  
Brown, C. P., 195  
Brooks, E. R., 310  
Brown, G. E., 359  
Brown, R. O., 595  
Brown, W. D., 341

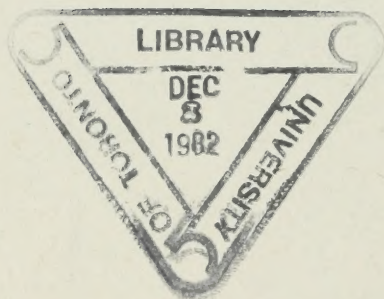
- Brown, W. L., 453  
 Brown, T. R., 601  
 Burekhardt, J. L., 66  
 Burnam, C. F., 440  
 Cade, 569  
 Cameron, M. H. V., 405  
 Carle, J., 207  
 Carman, R. D., 539  
 Carter, C. F., 236  
 Cary, E. G., 108  
 Cassini, 24  
 Cecil, R. I., 134  
 Chacko, M. P., 242  
 Charpin, 204  
 Chase, C. S., 581  
 Cheney, H. E., 497  
 Cheney, W. F., 535  
 Christian, H. A., 340  
 Clough, H. D., 330  
 Cohen, S. S., 57  
 Cole, A. C., 227  
 Colwell, H. S., 130  
 Connor, J. L., 84  
 Cooper, P. R., 248  
 Cordier, M., 487  
 Corper, H. J., 33  
 Cotton, T. F., 362  
 Covey, G. W., 287  
 Cowie, D. M., 91  
 Crocket, J., 37  
 Crohn, B. B., 503  
 Crump, E. S., 10  
 Culver, H., 475  
 Cummings, R., 351, 352  
 Darling, S. T., 574  
 Davison, W. C., 127, 130  
 D    , F., 348, 598  
 Devic, 364  
 Dock, G., 415, 522  
 Donald, W. G., 33  
 Doubourg, E., 116  
 Dragstedt, A., 581  
 Dragstedt, L. R., 581  
 Drinker, C. K., 371, 387  
 Dudgeon, L. S., 200  
 Durrieux, 542  
 Duval, C. W., 67  
 Eddy, N. B., 414  
 Edmondson, R. B., 564  
 Eichhorst, H., 113  
 Einhorn, M., 552  
 Else, J. E., 595  
 Emmons, V. B., 130  
 Eyre, J. W., 106  
 Farah, N., 281  
 Finley, F. G., 348  
 Fishbaugh, E. C., 516  
 Flexner, S., 163  
 Fougrouse, H. L., 236  
 Frauenthal, H. W., 165  
 Frazier, 556  
 Friedman, G. A., 524  
 Funk, E. H., 39  
 Galli, G., 355  
 Gammons, H. F., 47  
 Gay, F. P., 99  
 Geiger, J. C., 182  
 Gestley, J. R., 160  
 Geyelin, H. R., 450  
 Gibson, H. G., 84  
 Giltner, L. T., 564  
 Giordano, D., 582  
 Glynn, E., 292  
 Goodall, J. R., 238  
 Goodman, E. H., 318  
 Goormaghtigh, W. T., 433  
 Gordinier, H. C., 365  
 Gradwohl, R. B. H., 236  
 Greenway, J. C., 130  
 Greig, E. D. W., 240  
 Haden R., 161, 234  
 Hamilton, J. H., 93  
 Hansmann, G. H., 383  
 Hare, H. A., 356  
 Harrington, F. E., 181  
 Harris, D. H., 99  
 Harris, W. H., 67, 428  
 Harrop, G. A., jr., 23, 95  
 Harrower, H. R., 396  
 Hart, L., 195  
 Hart, T. S., 140  
 Hartzell, T. B., 484  
 Haughwout, F. G., 208  
 Havens, L. C., 126  
 Hawn, C. B., 197  
 Head, G. W., 136  
 Hearne, K. G., 606  
 Heiman, H., 192  
 Herrick, W. W., 149, 172  
 Herrmann, G. R., 203  
 Herrold, R. D., 475  
 Higley, H. A., 486  
 Hinkelmann, A. J., 71  
 Hinkelmann, C. P., 71  
 Hollande, 569  
 Holm, M. L., 127, 130

- Hopkins, J. D., 197  
 Howard, C. P., 383  
 Huck, J. G., 376  
 Hufnagel, 346  
 Innes, A., 608  
 Irvine, R. S., 100  
 Iwashima, S., 69  
 Jackson, J. B., 528  
 Johnson, W., 402  
 Johnston, J. L., 592  
 Kahn, M., 385  
 Kantor, J. L., 578  
 Karsner, H. T., 10, 13  
 Kennaway, E. K., 434  
 Kerr, W. J., 399, 420  
 Kickhefld, G., 118  
 Kime, E., 85  
 King, J. T., 50  
 King, O., 550  
 Kinsella, R. A., 70  
 Knowlton, R. H., 579  
 Koeckert, H. L., 13  
 Kofoed, C. A., 212  
 Kohman, F. F., 247  
 Kilmer, J. A., 79  
 Kornhauser, S. I., 212  
 Kretchmer, H. L., 481  
 Kristjanson, H. T., 389  
 Kuh, S., 400  
 Labbé, M., 211  
 Lamy, 364, 600  
 Landsmann, A. A., 587  
 Langmann, A. G., 292  
 Lantin, P. T., 208  
 Leconte, M., 311  
 Leonard, A. H., 93  
 Letulle, 346  
 Leven, G., 500  
 Levine, E. C., 377  
 Levine, S., 398  
 Lewis, J. H., 14  
 Lewy, 199  
 Leyton, O., 455  
 Lind, W. A. T., 605  
 Litchfield, L., 159  
 Litchfield, W. F., 558  
 Loeper, M., 558  
 Louers, A., 63  
 Lowe, E. C., 106  
 Lucke, B., 85, 302  
 Lüdin, 599  
 Lyal, H. W., 73  
 Lyon, M. W., Jr., 88, 258  
 MacIntyre, H. R., 51  
 Mackenzie, J., 111  
 Macleod, N., 237  
 Malloch, A., 343  
 Mandlebaum, F. S., 390  
 Mateer, J. G., 64  
 Maury, J. M., 488  
 Mayo, W. J., 477  
 McCarrison, R., 430  
 McClellan, J. H., 143  
 McClintock, J. T., 581  
 McClure, C. W., 492  
 McCoy, G. W., 104  
 McCrae, T., 39  
 McGregor, J. K., 408  
 McKinstry, W. H., 590  
 Meader, E. M., 197  
 Meakins, J., 334  
 Means, J. H., 423  
 Medalia, L. S., 98  
 Megaw, J. W. D., 226  
 Mertz, H. O., 464  
 Mills, C. H., 181  
 Minaker, A. J., 100  
 Mix, C. L., 292  
 Morris, M. F., 562  
 Morros, J. S., 590  
 Mottram, J. C., 434  
 Motzfeldt, K., 432  
 Mougeot, 331  
 Moynihan, B., 543  
 Neumann, L., 35  
 Neve, G., 117  
 Noguchi, H., 218, 219, 220, 221,  
     222, 224, 225  
 Nolf, 25  
 Nolf, P., 205  
 Norton, W. H., 247  
 Olitsky, P. K., 157  
 Orticoni, 65  
 Osborne, O. T., 120  
 Otterman, A., 594  
 Paillard, H., 513  
 Paiseau, G., 187  
 Palfrew, F. W., 195  
 Parkhurst, G. M., 172  
 Parkinson, J., 321  
 Parturier, 542  
 Philibert, A., 42  
 Philips, H. B., 292  
 Pickard, R. J., 566  
 Pollock, R., 566  
 Pottenger, F. M., 45, 53, 303



- Poynton, J., 167  
 Pron, L., 518  
 Purdy, W. C., 182  
 Ramirez, M. A., 265  
 Ransom, B. H., 285  
 Rappley, W. C., 472  
 Ravaut, 204  
 Raw, N., 30  
 Rawnsley, G. T., 190  
 Ray, M. H., 302  
 Regan, C., 243  
 Regan, J. C., 243, 245  
 Reiss, J., 503  
 Rhea, L. J., 343  
 Rice, E. L., 427  
 Riley, W. A., 568  
 Rivenbaugh, W. T., 140  
 Roberts, D., 108  
 Rodet, A., 193  
 Robinson, G. C., 336  
 Robinson, G. H., 149  
 Robison, J. F., 160  
 Rogers, L., 381  
 Rolleston, H., 146  
 Rosenblatt, J., 512  
 Rosenow, E. C., 101  
 Rothschild, L., 10  
 Roussy, B., 75  
 Sahli, H., 118  
 Sakakami, K., 69  
 Sailer, J., 312  
 Sainton, P., 169  
 Schiff, 199  
 Sellards, A. W., 228, 231, 233  
 Semple, D., 253  
 Shoemaker, H., 555  
 Siegrist, H., 527  
 Simonds, J. P., 289  
 Smith, 114  
 Smith, L. M., 474  
 Squier, T. L., 110  
 Solis-Cohen, S., 57  
 Stanton, F. M., 175  
 Stark, G. W., 479  
 Stillman, E. G., 77, 445  
 Stivelman, B., 115, 279  
 Stockton, C. G., 384  
 Stoll, H. F., 35  
 Stone, M. C., 341  
 Stone, R. L., 191  
 Stone, W. J., 151, 296, 345  
 Studebaker, J. F., 49  
 Sturdivant, B. F., 101  
 Sturgis, C. C., 325, 328  
 Sturm, E., 231  
 Sutherland, G. A., 337  
 Swezy, O., 212  
 Taylor, F. E., 610  
 Tenney, C. F., 140  
 Thom, C., 564  
 Thomson, J. G., 181  
 Thro, W. C., 274  
 Tompkins, E. H., 328, 330, 387  
 Topp, V., 355  
 Tracker-Neville, W. S., 76  
 Trist, M. E., 79  
 Truitt, R. C. P., 151  
 Upham, R., 486  
 Vanderhoof, D., 505  
 Vargas, J., 38  
 Vaughan, H. F., 134  
 Venning, J. A., 324  
 Vrowe, S. J., 76  
 Wahl, H. R., 73  
 Walker, I. C., 266, 269  
 Wang, C. Y., 37  
 Ward, E., 32  
 Warfield, L. M., 331  
 Wearn, J. T., 325, 328, 330  
 Weaver, G. H., 27, 162  
 Weber, F. P., 249, 260  
 Weiss, C., 124  
 Wentworth, A., 233  
 Whipple, G. H., 469  
 White, A. W., 584  
 White, G. B., 73  
 Wiel, 309  
 Wight, T., 85  
 Wildbolz, H., 49  
 Wilkins, W. A., 42  
 Wilkinson, G. R., 156  
 Wilson, J. A., 15, 80  
 Wilson, W. J., 94  
 Winchell, A. I., 77  
 Wishart, M. B., 474  
 Wood, E. J., 604  
 Wolf, E. P., 14  
 Woolfe, M. S., 250  
 Wynn, W. H., 106  
 Yagel, E., 79  
 Yamanouchi, T., 69  
 Yates, J. L., 7  
 Yorke, W., 201  
 Young, C. F., 466





SERIAL

R

General medicine

101

Y39

1920

Neurological

Medical

Serials

